The New England
Journal of Medicine

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VOLUME 221 DECEMBER 28, 1939 NUMBER 26

EMPYEMA IN CHILDREN*

THOMAS H. LANMAN, M.D.,† AND HENRY L. HEYL, M.D.‡

BOSTON

THE successful treatment of acute empyema thoracis depends on so many variable factors that it is extremely difficult to evaluate the results in any single series. For the same reason, the comparison of series of cases treated by different men at different institutions is also difficult. More accurate conclusions may be drawn from the analysis of the results obtained from an individual institution. Especially is this true if the number of cases is adequate, the direction of treatment is to all intents and purposes in the same hands and each period covers a number of years.

This report presents a further analysis of the cases of empyema operated on at the Children's Hospital in Boston. Three previous reports from this hospital (Ladd and Cutler[1, 2] and Hudson[3]) go through the year 1928. From January, 1929, through December, 1938, there were 287 additional cases. This brings the total to 468 cases, but it is with the recent group of cases that this paper is primarily concerned.

Statistically the recent series shows nothing striking as regards the incidence of sex or of the involvement of one thoracic cavity over the other. Boys comprised 59 per cent of the patients, and girls 41 per cent. The left side was involved in 58 per cent of the cases, the right side in 40 per cent and both sides in 2 per cent.

ETIOLOGY

The predominating etiologic organisms and the mortality in each group are shown in Table 1. As was to be expected, the pneumococcus was the invading organism in the great majority of cases — 80 per cent. *Staphylococcus aureus* and *Streptococcus hemolyticus* were each responsible for about 10 per cent of the total cases, with the streptococcus showing the highest mortality of the three groups — 33 per cent. Other organisms were found predominant in 0.6 per cent of the series.

MORTALITY BY AGE GROUPS

It is well recognized and has been pointed out by many authors that the mortality in empyema is exceedingly high in children of two years of age or under. As will be noted in Table 2, the mortality in this age group was about the same in the first and second five-year periods — 35 and 33 per cent, respectively. There was a decrease to 21 per cent in the third five-year period and a very gratifying drop to 4 per cent in the last. The mortality for all ages remained at about 13 per cent for the first three of the five-year groups but showed a very gratifying drop to 2 per cent in the last.

TABLE 1. *Relation of Predominant Organism to Mortality.*

PREDOMINANT ORGANISM	ALL CASES	MORTALITY
	%	%
Pneumococcus	80.0	2.9
Streptococcus hemolyticus	10.4	33.0
Staphylococcus aureus	9.0	11.0
Other organisms	0.6	

TABLE 2. *Results of Treatment of Empyema in Children (1919–1939).*

FIVE-YEAR PERIOD	ALL CASES			PATIENTS TWO YEARS OR UNDER		
	NO. OF CASES	NO. OF DEATHS	MORTALITY	NO. OF CASES	NO. OF DEATHS	MORTALITY
			%			%
1919–1924	94	13	14	20	7	35
1924–1929	86	11	13	21	7	33
1929–1934	150	20	13	57	12	21
1934–1939	137	3	2	46	2	4

It is admitted that the drop in the mortality in the last five-year period may have been influenced by the virulence of the infecting organisms during that period, but in large part it was due to more efficient handling of individual cases. Although mortality varies from year to year according to the virulence of the organisms in any given year, it also depends to a considerable de-

*Read at the annual meeting of the New England Surgical Society, September 29, 1939.
From the Surgical Service, Children's Hospital, Boston, and the departments of surgery and pediatrics, Harvard Medical School.

†Visiting surgeon, Children's Hospital; assistant professor of surgery, Harvard Medical School.

‡Assistant resident surgeon, Children's Hospital; assistant in surgery, Harvard Medical School.

gree on the form of treatment applied. If treatment is based not on the indications of the given case and on the infecting organism but on a routine that may have given success in a previous year, the results may be disastrous.

The controversy that has raged off and on since the World War over the relative merits of repeated aspirations, closed drainage and open drainage is the result of the tendency to fit a routine treatment to the patient rather than to modify the treatment according to the individual requirements of the patient. While it is possible that in the next five-year period at our hospital the mortality will rise, it is believed that comparisons of five-year periods each covering a large number of cases are sufficient to minimize the errors which would result from analyzing smaller series taken year by year. In the last five-year period of the series here covered, 1 death occurred in 1935 and 2 in 1934. In 1936, 1937 and 1938 there were 84 cases of all ages but no deaths. This does not include cases undiagnosed before autopsy, or those in which death was due to some other acute primary disease.

Forms of Treatment

There are three recognized forms of treatment: aspiration, intercostal closed drainage and open thoracotomy, with or without rib resection. It is of fundamental importance to realize that each of these has its sphere of usefulness, its limitations and its contraindications, and that stubbornly to advocate or adhere to any one of them for all cases is to invite disaster.

Aspiration

There is one form of treatment of empyema which is applicable at least in part to all cases, namely aspiration. Its high practical value, regardless of the form of drainage that may be selected, lies in furnishing knowledge of the invading organism, and it should therefore be used in all cases at the start of treatment. In addition to supplying valuable laboratory data, it is of decided advantage in that it relieves mechanical embarrassment due to the accumulation of fluid in the pleural cavity with a minimum of handling and manipulation, especially during the syn-pneumonic stage. With proper infiltration of the skin by novocain, aspiration can be accomplished with a minimum of discomfort and without moving the patient from bed. In very sick patients in the syn-pneumonic stage, whether the responsible organism be the streptococcus, the staphylococcus or the pneumococcus, it is essential to understand that the accumulation of fluid in the pleural cavity is only one manifestation of the disease. Unless the fluid is sufficient to cause mechanical embarrassment of the heart or lungs, its presence is of relatively slight significance to the welfare of the patient. Therefore measures for its removal should never be undertaken by such means as will throw an undue added strain on a patient already critically ill. By the same token, at this stage the fluid, whatever the responsible organism may be, is still thin enough to permit its easy removal by aspiration, if removal in a quantity greater than that needed for diagnosis be indicated.

It will perhaps be pertinent to compare acute empyema during the syn-pneumonic stage with acute osteomyelitis. The latter disease in children under two years of age at this hospital twenty-five years ago showed a distressingly high mortality — about 50 per cent. Its mortality in this age group is now between 5 and 10 per cent, very largely because it has been recognized that the lesion in the bone is but one manifestation of a severe and generalized infection. The sick child who has pneumonia and, in addition, fluid in the pleural cavity is now treated as a whole rather than with attention and efforts unwisely focused on the drainage of the fluid. And, as in acute osteomyelitis, when drainage is undertaken it is accomplished by means that give the minimum of trauma and manipulation, even though good "surgical drainage" may not at that time be established.

Intercostal Closed Drainage

Intercostal closed drainage is particularly to be advised in cases where the reaccumulation of fluid after aspiration is so rapid that even daily aspiration fails to give adequate relief. It provides continuous drainage, does away with the discomfort of repeated aspirations and can be accomplished satisfactorily without moving the patient from bed. In many cases, especially those in which the infection is due to the streptococcus, it results in cure. The technic of instituting this form of drainage does not matter to any significant degree, provided certain principles are observed. The wound must be small enough for the drainage tube to fit snugly; the usual precautions against allowing air to enter the thorax must be observed; the tube must not be inserted too far within the chest. We have had success with comparatively simple forms of apparatus. In performing the thoracotomy we use a trocar and cannula. A soft-rubber catheter is inserted through the cannula after the trocar has been withdrawn. After removal of the fluid — and this should not be done too rapidly — the catheter is connected with another section of rubber tube, the distal end of which is

placed under water in a container at a lower level than that of the patient's body.

In spite of many claims to the contrary, it is our belief that there is no form of closed drainage that stays absolutely airtight for more than a week or two. Also, the necessity for airtight drainage for a longer period than two or three weeks is seldom if ever sufficiently important to be of any consequence. Some years ago an attempt was made for two years to determine the relative value of closed drainage with and without tidal irrigation. The advantages of tidal irrigation are several, but to administer it successfully requires the almost constant attendance of a highly trained and unchanging personnel. Under conditions as nearly optimum as could be obtained, the results of these two kinds of closed drainage, as used in alternate cases during the two-year period, showed no appreciable difference either in the length of time spent in the hospital or in the lessening of complications. Tidal irrigation has therefore been abandoned, since its technical disadvantages appear to outweigh any slight advantages that it may possess. The simpler the form of apparatus the better. So far as irrigation is concerned, attention is directed to preventing the tube from becoming clogged. If after a week or two, particularly in pneumococcal infections, the intercostal tube is not providing adequate drainage, the condition of the patient should by that time be sufficiently improved to warrant open surgical drainage.

The value of intercostal closed drainage is particularly great in early cases and in young patients. Much of the condemnation of drainage by rib resection has been wrongly attributed to the operation rather than to the choice of case in which it is used. Primary open operation, with or without rib resection, should seldom if ever be employed for patients under two years of age, and should never be employed during the synpneumonic stage, regardless of age. This fact is well recognized, but we wish also to emphasize that in many cases long-continued attempts to obtain adequate drainage by closed methods should be abandoned and open drainage substituted. Enough patients have come to the Children's Hospital with chronic empyema after weeks and even months of inadequate drainage of the pleural cavity by intercostal tube to make us believe that such drainage should not be prolonged much over two or three weeks unless there is obvious evidence of improvement, as shown by clinical condition, decrease in the size of the cavity and re-expansion of the involved lung. The patient whose general condition has not improved sufficiently to warrant open drainage after two or three weeks of closed drainage is a rarity, and in such cases there is usually some other complicating factor, frequently a bronchopleural fistula.

Open Drainage

In properly selected cases, open drainage is one of the most efficient methods available for the treatment of empyema. As shown by Table 3,

TABLE 3. *Efficiency of Surgical Treatment in 243 Recovered Cases of Empyema.*

TYPE OF TREATMENT	NO. OF CASES	AVERAGE DURATION OF POSTOPERATIVE DRAINAGE
		days
Rib resection	168	24
Intercostal drainage	39	40
Intercostal drainage followed by rib resection	36	57

primary rib resection was used in this series in 168 cases out of 243. These were uncomplicated cases which ended in complete recovery. The average hospital stay after drainage had been instituted was twenty-four days, in comparison with forty days for the cases receiving intercostal drainage, and fifty-seven days for those receiving intercostal drainage followed by rib resection. We cannot agree with the opinion that rib resection is an improper form of treatment. Judging from our experience, its chief danger is the unwise selection of cases for its use, particularly as regards the stage of the disease when drainage is to be instituted. In the last five years there has been only 1 death — in a boy of five — where primary rib resection was done. In this case death occurred suddenly thirty-five days postoperatively from what was supposed to have been an embolus, although no postmortem was obtained. In any event it is hardly fair to attribute the death to the fact that rib resection had been done thirty-five days previously. There was one other death following primary rib resection in the last five-year period. This patient was less than a year old, and we believe that the choice of drainage was an error of judgment, although the infant had recovered from the pneumonia and was apparently in excellent shape, and the pus was of the thick pneumococcal type. In the last two five-year periods there were 3 deaths following primary rib resection in children two years of age or younger. These might have been avoided had the less radical method of intercostal drainage been adopted as a preliminary step. It is probable that overconfidence in rib resection had resulted from our success with it. Good as these results were, they might have been even better had we adopted our rule of today of doing no primary

rib resections in patients under two or three years of age.

Rib resection is always preceded by a diagnostic tap in order to determine the organism. The ideal case for primary rib resection is that of a child at least two years old, preferably over three, in a fairly good state of nutrition, who has recovered from pneumonia at least a week previously. Particularly if the responsible organism is the pneumococcus and the fluid is thick and full of fibrin will this method be most effective. In such a case the mediastinum is well fixed, the child is not toxic and the open operation permits the operator to free the lung, and in many cases to remove at that time the large masses of fibrin. A double-flanged rubber empyema button is used, and we rely on the respiratory movements of the freed lung to promote free drainage and obliteration of the cavity. There are only rare cases in which irrigation of the cavity is desirable. The child is not acutely ill and he is encouraged to sit up in bed and be active, and after a few days to be up and around the ward. The use of blow bottles or some similar apparatus to promote expansion of the lung is advocated. The empyema button is seldom left in place for more than fourteen days. The clinical condition of the child and the appearance of the cavity under x-ray are the most reliable guides for prognosis during convalescence.

It is appreciated that many of our patients who received primary rib resections were referred to the hospital when they were well over their pneumonia. For this reason, such a large percentage of primary rib resections would not, and probably should not, be found in a series of cases in private practice. Paradoxically, however, this large group of patients, who had a primary rib resection and whose hospital stay was materially shorter than that of the patients receiving intercostal drainage, with or without rib resection, may have received better treatment of their empyema than patients observed from the start of their pneumonia. In other words, because of failure of early diagnosis of the fluid in the chest the necessity for surgery was realized at more nearly an optimum time than is often true of patients in a better economic status. The typical history in these cases was that the child had had a "cold," with cough, high fever and pain in the chest. Pneumonia may or may not have been diagnosed, and the child was kept in bed for a week or ten days. Later the fever recurred and the child was referred to the hospital for possible empyema. Often only one or two visits had been made by a physician. This sort of medical attention is of course not advocated, but the facts here stated deserve at least close consideration, and certainly confirm our opinion that the surgical drainage of acute empyema is seldom if ever a surgical emergency.

Site of Drainage

The best place for incision depends of course on the location of the pus. Drainage of the pus-filled cavity in its most dependent portion is desirable, but it must be borne in mind that if the incision is made too low the diaphragm will tend to rise against the drainage tube as the cavity becomes emptied. This is of particular importance in cases that are receiving intercostal drainage and in which open drainage may be required later. It is seldom desirable to resect a rib lower than the eighth, and the seventh is usually preferable. In the great majority of cases the posterior axillary line is the best. If the intercostal drainage has been done in the eighth interspace, it may be found at the time of rib resection that the removal of the eighth or ninth rib will give inadequate drainage since the diaphragm has ascended to that level. We have had the experience on one occasion of going through the diaphragm under these conditions. While no harm was done, it was at least humiliating.

Cause of Death

The occurrence of operative deaths and those following shortly after surgical drainage should make one consider carefully whether or not the surgical procedure was more radical than the case justified. There must, however, be many cases in which the patient dies not because of the empyema but with empyema. Although such cases are included in this series, it is perhaps unfair to attribute a death to empyema when this forms only part of the evidence of a systemic infection. A patient who has had pneumonia, empyema, purulent pericarditis, mastoiditis and a positive blood culture for *Streptococcus hemolyticus* dies of the general septicemia and not of any one manifestation of the infection.

Anesthesia

Aspiration, whether exploratory or for drainage, can be accomplished easily under novocain infiltration, and should be. Local anesthesia is feasible in most cases that require intercostal closed drainage, although at times a supplementary, light, nitrous oxide and oxygen anesthesia is helpful and is seldom contraindicated. In the occasional case where a brief general anesthesia is needed for a sick patient, cyclopropane is a valuable anesthetic agent. For open thoracotomy, especially in cases requiring rib resection, a general anesthetic is preferable. If the patient is not in suita-

ble condition to withstand a general anesthetic, these more radical forms of drainage should not be used. For rib resection, nitrous oxide and oxygen is as a rule the anesthetic of choice.

Scoliosis

Our experience with rib resection as well as with intercostal drainage leads to the firm belief that permanent structural scoliosis will seldom if ever result if the empyema cavity has been properly drained, thereby resulting in its obliteration and in complete re-expansion of the lung on the affected side. It is recognized that postoperative x-ray films taken during convalescence when the cavity has not yet been obliterated may show some degree of scoliosis. Our results, however, confirm the impression that endeavors should be made at this time to favor drainage and re-expansion of the lung. If the child is permitted to be as active as his condition warrants, this will aid and hasten re-expansion of the lung and obliteration of the cavity. The scoliosis will then disappear. Therefore active methods advocated for the treatment of scoliosis at this time are contraindicated. If the child is placed on a Bradford frame or some other form of apparatus in order to correct the apparent scoliosis, the immobilization hinders and may even defeat Nature's usually successful efforts to overcome what is only a functional and not a true structural scoliosis.

Chronic Empyema

It is beyond the scope of this paper to deal with chronic empyema, but it is pertinent to point out that the best preventive of the condition is adequate treatment during the acute stages of the disease. The incidence of chronic empyema in cases under observation from the start in our hospital is becoming as gratifyingly small as is the mortality in the acute cases.

Chemical Therapy

The use of sulfanilamide and sulfapyridine can receive only a few words here. While a few patients with streptococcal pneumonia and empyema received sulfanilamide during 1938, the number is too small to permit any reliable conclusions as to the efficiency of the drug in preventing or treating empyema. Sulfapyridine was not given in any of the cases here considered, but during 1939 a few patients received it. Admitting the value of the drug in acute pneumonia, it is proper to sound a note of caution against continuing its use when the complication of empyema has arisen. No definite statement can be made, but we are under the distinct impression that the pleural exudate in some of the few cases of empyema which have developed during treatment with sulfapyridine has been more difficult to drain. It has been of a thick, tenacious character, with very little fluid present, and a rather wide exposure, with thorough freeing of the lung, was necessary. The patients as a rule were slow in recovering, but time alone will assign the true value to the use of this drug.

Summary and Conclusions

An analysis of the treatment of empyema thoracis during the last twenty years is presented. Comparison of mortality statistics of four five-year periods shows a gratifying drop in mortality, not only in older children but also in infants. The following conclusions seem justified, though it is realized that many of them have previously been made not only by those in our hospital but by others:

Acute empyema should never be regarded as a surgical emergency.

Children, especially those two years of age and under, die with empyema and not because of it.

Empyema must be treated as a complication of a general systemic infection.

The child as a whole must be treated, not merely the condition in the pleural cavity.

The recent improvements in preoperative and postoperative care, particularly from the point of view of fluid balance, are of great importance.

Diagnostic thoracentesis should be done in all cases in order to determine the organism.

The type of drainage instituted must be based on the needs of the individual case. The simpler the form of apparatus used the better.

Primary open drainage, with or without rib resection, should never be done during the synpneumonic stage or in children under two years of age. If the patient's condition contraindicates a general anesthetic, methods of drainage requiring a general anesthetic are also contraindicated.

In properly selected cases, primary rib resection is a safe and most efficient method of treatment.

Local anesthesia for aspiration and intercostal closed drainage, and nitrous oxide and oxygen for open drainage, are favored.

Scoliosis need not be feared if the empyema is well drained and the cavity is obliterated by the expanded lung.

The treatment of empyema requires the closest co-operation between the surgeon, the internist and the roentgenologist.

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Discussion

Dr. Allen G. Rice, Springfield, Massachusetts: Those of us who recall the treatment of empyema in the days of the World War realize the lessons that we have learned since then. These have evidently stuck, and all that remains for me to do is to emphasize certain points which were brought out by Dr. Lanman.

In the first place, the presence of empyema does not constitute an emergency; in the second place, one must not be in a hurry to operate on those who have it. My former chief in the Boston City Hospital, Dr. Gavin, was always urging us not to operate on cases of empyema until they were "ripe," by which he meant until there was thick pus. In the meantime, he advised continued aspiration.

The third point, which seems to me equally important, is that the surgical procedure should fit the patient. No one operation will cure all such cases, and proper selection and conduct of the operation have more to do with the eventual outcome than any other factors.

Aspiration, it seems to me, is the first thing to be done, and it should be repeated. Rib resection is to be considered a last resort, especially in children.

Recently a young surgeon came to Springfield who is specially trained in chest work, and the tendency is to turn over all such cases to him. So far this practice has proved worth while, and we have every reason to believe that what little mortality exists will decrease in this surgeon's hands. I believe that these cases can be handled much better by one man than when they are divided among several general surgeons.

Dr. Bancroft C. Wheeler, Worcester, Massachusetts: Dr. Lanman has covered his subject both clearly and completely. With so large a series of cases to support his conclusions, they bear the stamp of authority. I should like to emphasize briefly three of the points he has brought up.

In the first place, he said that surgical drainage of acute empyema is rarely an emergency. He believes that harm is more likely to result from doing a rib resection during active pneumonia than from delaying it an unnecessarily long time after empyema has developed. He presented as partial evidence the lower mortality rate and shorter convalescent period in a series of cases admitted to the hospital late in the course of the disease. Secondly, with regard to the value of irrigation he expresses frank skepticism. This is a far cry from the rigid Dakin's technic that was widely adhered to for some years after the last war, and is an agreeable simplification. Thirdly, his preliminary observations on the nature of the exudate in cases following pneumonia treated with sulfapyridine are interesting. It has been well established that neither sulfanilamide nor sulfapyridine is of much value in the treatment of such localized, walled-off pus pockets. But they are both effective in reducing the mortality of the commoner forms of pneumonia, and thereby presumably the incidence of empyema. It seems probable that the next ten years will see only a fraction of 287 cases of empyema at the Children's Hospital.

I shall present our experience with empyema in children at the Worcester Memorial Hospital during the last ten years. The series is of course much smaller than that of the Children's Hospital, but may be of interest as illustrating the occurrence and treatment of the disease in a medium-sized general hospital.

Between 1929 and 1938, there were 42 cases of empyema in children. Twelve were in infants, and 30 in children from three to twelve years of age. Of the total, 25 cases were directly due to pneumococcus; 6 to streptococcus and 4 to staphylococcus, while 5 were caused by a mixture of pneumococci and streptococci and 2 by a mixture of staphylococci and streptococci. In all but 3 the primary focus was pneumonia.

Twenty-four of these cases of empyema were treated by open drainage; 17 by closed drainage and 1 by aspiration only. Aspiration was used, however, for diagnosis in all cases and as a part of treatment in many. The case treated by aspiration alone proved fatal, as did 3 of those treated by closed drainage. The time in the hospital after drainage varied from ten days to six and a half months, but 80 per cent of the 38 living patients were discharged in six weeks or less.

Of the 4 fatal cases, 2 had a trocar thoracotomy performed during the course of active streptococcal pneumonia, 1 with a positive blood culture, and might have fared better if aspirations had been continued for a longer period. A third patient, admitted on the tenth day of pneumonia, died on the third hospital day, following two aspirations. The fourth case was that of a two-and-a-half-year-old child who had been ill for three weeks. Aspiration was unsuccessful because of the tenaciousness of the pus, and the patient died, in spite of a thoracotomy; on postmortem examination meningitis was found to be present.

Dr. George A. Moore, Brockton, Massachusetts: I am interested to know what Dr. Lanman's experience has been with sulfapyridine in empyemas due to pneumococci. During the past winter I saw two patients with pneumococcal empyema who had been treated successfully with sulfapyridine during the pneumonia which preceded the empyema. Both cases were treated by aspiration in the early days of the development of empyema, with no untoward results. When it became necessary to resort to catheter drainage, both patients had a rather marked rise in temperature, which was controlled by the use of sulfapyridine, and both made satisfactory recoveries.

Dr. Richard H. Overholt, Boston: I should like to add my approval of the general practice and plan that Dr. Lanman has outlined for the various procedures. I should like to ask whether a study has been made of symptoms in the patients in this series which might indicate the nature of the underlying pulmonary lesion. We are too often asked to see patients who have developed bronchiectasis or occasionally bronchial fistulas following treatment, and in view of the excellent results reported, I am curious to know how many patients developed bronchopleural fistulas or evidence of bronchiectasis or pulmonary abscess that might require a subsequent resection of the involved pulmonary tissue.

Dr. Lanman: In answer to the question regarding treatment with sulfanilamide and sulfapyridine, I will say that no cases in this series were so treated. Sulfapyridine had not come into use until after its close. However, we have since that time had 6 cases of empyema developing in patients who had been treated with sulfapyridine during their pneumonia. In 4 cases the exudate in the lung was very thick and was difficult to clear up. In 1 case, as soon as the administration of sulfapyridine was stopped the temperature went up but came down when the drug was resumed. This continued for about six weeks, when it became necessary to do a very wide and open drainage. As a result, the empyema finally cleared up.

I did not say much on this subject because we have not as yet collected sufficient evidence of the value of sulfapyridine in empyema, or any accurate figures as to how

many patients develop empyema when they have had either sulfanilamide or sulfapyridine during the course of their pneumonia.

In answer to Dr. Overholt's question, this series did not concern itself with cases of bronchiectasis. I have been unable to find in the series of cases treated by primary rib resection any that developed symptoms suggestive of communicating pulmonary infection. We are now studying the records in a large series of cases of pneumonia with special attention as to whether there was at the time of the pneumonia some unrecognized atelectasis. Some of these patients had empyema associated with the pneumonia, but many others did not. On the evidence we now have at hand, it would seem that the development of bronchiectasis is more likely to be the result of an unrecognized atelectasis than of the empyema. We realize of course that there are many other factors, some as yet unknown, that cause bronchiectasis. Cases of pneumonia with empyema that have been complicated by lung abscess or bronchial fistula may go on to chronic pulmonary suppuration.

ROULEAUX FORMATION IN FRESH, UNMODIFIED BLOOD AS A DIAGNOSTIC TEST FOR HEMOLYTIC ANEMIA*

WILLIAM DAMESHEK, M.D.†

BOSTON

IN THE course of recent studies on the nature of the hemolytic anemias, it was demonstrated that spherocytosis of the red blood cells was in most cases a constant feature.[1, 2] Further studies now in progress indicate that this tendency of red cells to become small, thick and spherical is dependent on the action of various hemolytic agents on mature erythrocytes, and not on an abnormal formation of red cells in the bone marrow.[3] Spherocytosis may thus be considered an indicator of hemolytic activity. This abnormality is by no means pathognomonic of congenital hemolytic jaundice, being found in various hemolytic syndromes.[4] Previous studies by Haden,[5] Boros,[6] Heilmeyer[7] and Castle and Daland[8] have shown that the spherocyte is a fragile red blood cell, and that its behavior in hypotonic solutions of sodium chloride can be directly correlated with its thickness. As the cell becomes thicker its diameter diminishes, although its volume remains constant. Various methods have been utilized for the estimation of the degree of spherocytosis or increased thickness of the average red blood cell. Thus the mean corpuscular thickness is determined from the knowledge of three factors: the hematocrit reading, the erythrocyte count and the mean diameter of the cell. Thus:

$$\text{Thickness} = \frac{\dfrac{\text{Hematocrit reading} \times 10}{\text{Red blood cells in millions}}}{\pi \left\{ \dfrac{\text{Cell diameter}}{2} \right\}^2} = \frac{\text{Mean corpuscular volume}}{\text{Mean corpuscular area}}$$

An example for a normal blood is as follows:

$$\text{Thickness} = \frac{\dfrac{46 \times 10}{5.0}}{3.14 \left\{ \dfrac{7.5}{2} \right\}^2} = \frac{92}{44} = 2.1 \text{ microns}$$

The normal mean corpuscular thickness is about 2 microns. Heilmeyer[7] makes use of the thickness: diameter (T:D) ratio in expressing the degree of thickness. This index serves graphically to illustrate increases in thickness of the red cell. The normal T:D: ratio is about 1:4; with spherocytosis this ratio becomes abnormal and may reach

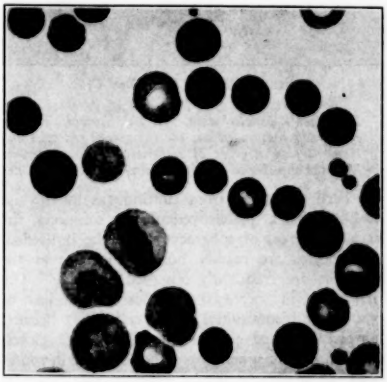

FIGURE 1. *Cells from a Case of Acute Hemolytic Anemia. Photomicrograph of a stained blood smear. The small, dense-appearing red cells, usually without central achromia, are spherocytes. The contrast in the size of these cells as compared with the comparatively large reticulocytes is readily apparent.* (× 1350.)

levels of 1:2.5 or 1:2. Another method of estimating thickness indirectly is by performing the fragility test with solutions of hypotonic sodium chloride.

Direct observation of red cells for thickness has not been utilized so often as it should, and it is the purpose of this paper to point out the useful-

*From the Hematology Laboratory, Beth Israel Hospital, Boston. Aided by grants from the Proctor Fund, Harvard Medical School, and the Charlton Fund, Tufts College Medical School.

†Assistant professor of medicine, Tufts College Medical School; instructor in medicine, Courses for Graduates, Harvard Medical School; physician and chief of Blood Clinic, Boston Dispensary.

ness of this procedure. Although a stained preparation demonstrates certain characteristics of the spherocyte, namely diminished size, absence of central clear space and an increased depth of coloration (Fig. 1), it can give only presumptive information. In a fresh preparation of blood which

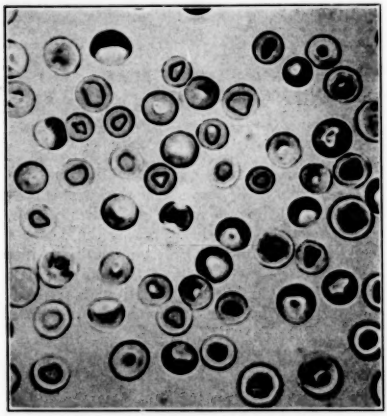

FIGURE 2. *Normal Red Blood Cells.*

Photomicrograph of a fresh wet preparation, using Dameshek's platelet stain. In this isotonic solution containing sodium citrate, the individual red cells and their varying degrees of thickness can be observed. Note the cup-shaped and spherical red cells. (× 1000.)

has been prevented from clotting (as by the use of Dameshek's[9] platelet-reticulocyte solution), the various degrees of spherocytosis in the individual erythrocytes are readily noted (Fig. 2), as the red cells are frequently observed on edge. The first stage in increased thickness is the loss of one of the biconcavities of the cells; they become cup-shaped, then jug-shaped. The stage closest to the complete spherocyte is that of a small, round cell with a dimple at one end; the final stage is that of complete spherocytosis (microcytosis).*

A simpler method, and one which often gives somewhat more information, especially as regards thickness and the thickness-diameter relation, is the observation of rouleaux formation in fresh preparations of blood. When a drop of blood is placed on a cover slip, which is then dropped on a slide, the red cells form aggregates, or rouleaux, consisting of a varying number of cells in close approximation and resembling a pile of coins. The size of the aggregates and the closeness of the approximation depend in large part on the chemical status of the serum.† In the process of aggregation the pliable red cells apparently lose one of their biconcavities, so that one cell fits snugly into the concave portion of its neighbor. Close inspection of the rouleaux reveals that the cells are quite uniform in thickness, although some variation in size is readily apparent (Fig. 3). From photomicrographs one may readily measure the thickness of the individual cells in relation to the diameter of certain free floating cells which are viewed from above. This ratio, as stated above, is normally about 1:4.

In the presence of spherocytosis the rouleaux always become abnormal. This is due to the great diversity in the thickness of the red cells and the resulting difficulty of individual cells' becoming approximated to each other. Because of this the rouleaux are hardly ever straight, rarely lengthy and often decidedly bizarre in appearance (Figs.

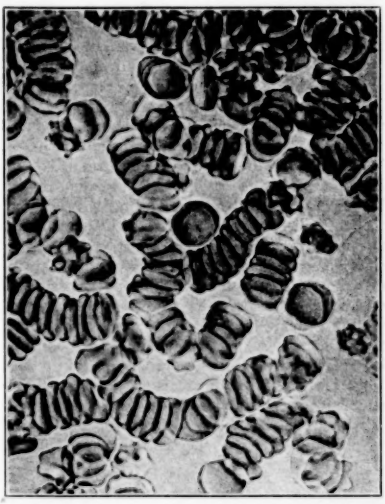

FIGURE 3. *Rouleaux Formation in Normal Blood.*

Photomicrograph of a fresh wet preparation. Note the long rouleaux and the approximate equality in thickness of the erythrocytes. The thickness:diameter relation can be estimated by direct measurements. (× 1000.)

4 and 5). The difficulty of an almost spherical cell's being closely approximated to other cells which are also thickened and rounded is obvious, and reminds one of a number of fat people trying

*The observer can readily reproduce these changes by making a fresh preparation of blood on a slide on which has been placed a pinch of pure saponin.

†The interesting relation of the size of the rouleaux to the fibrinogen content of the blood serum and to the blood sedimentation rate has recently been discussed.[10, 11]

to get into a small elevator. Individual and comparative variations in erythrocyte thickness are exceptionally well brought out in these fresh preparations.

This simple test, which can be made at a moment's notice with a minimum of apparatus (glass slides and cover slips), has proved of definite value in the differential diagnosis of certain cases of anemia, particularly those in which the possibility of a hemolytic process is present. It often yields immediate information regarding such factors as the degree of spherocytosis (and indirectly of the probable erythrocyte fragility), and is thus of value in gauging the acuteness of the hemolytic process. Similar observations have recently been made by Gripwall.[12] The more fulminating a given hemolytic process, the more marked is the spherocytosis.[2] This is well brought

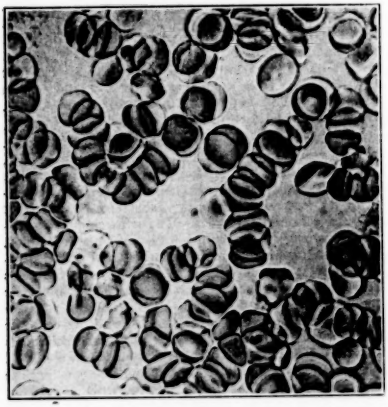

FIGURE 4. *Rouleaux Formation in a Case of Congenital Hemolytic Jaundice.*

Photomicrograph of a fresh wet preparation. Careful inspection of various rouleaux demonstrates the generally increased thickness of the red cells and their great diversity in this factor. (× 1000.)

out in the crises of congenital hemolytic icterus. As a preliminary diagnostic measure the test has much to recommend it; it supplements and in no wise replaces the more exact, and exacting, methods of estimating the mean corpuscular thickness, the mean diameter of the red blood cells and their fragility. Studies are now being made to determine the value of the rouleaux test for the direct measurement of red-cell thickness.

SUMMARY

The study of rouleaux formation in fresh preparations of blood is of value in estimating the presence or absence of varying degrees of thickness (spherocytosis) of the red cells. Since this abnormality is common to various types of hemolytic syndromes, the study of rouleaux is important in the diagnosis of hemolytic anemia and in the estimation of the severity of a given hemolytic process.

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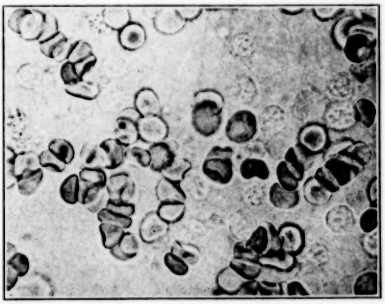

FIGURE 5. *Rouleaux Formation in a Case of Acute Hemolytic Anemia and Chronic Lymphatic Leukemia.*

Photomicrograph of a fresh wet preparation. Note the small, bizarre rouleaux, the marked variation in size and thickness of the red cells, and the many small thick cells. The colorless cells are lymphocytes. Observation of a smear of this type indicates the presence of a hemolytic process with increased erythrocyte fragility. (× 900.)

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THE SYNDROME OF DIABETES MELLITUS, HYPERTENSION AND NEPHROSIS*

A Clinical and Pathological Study of a Case

HARRY A. DEROW, M.D.,† MARK D. ALTSCHULE, M.D.,† AND MONROE J. SCHLESINGER, M.D.§

BOSTON

IN 1936, Kimmelstiel and Wilson[1] described a uniform pathologic lesion in the kidneys from a group of 8 middle-aged or elderly diabetic patients with hypertension who developed profuse albuminuria and generalized edema. They discussed the picture in sufficient detail to differentiate it clearly from other renal lesions. However, the discussion of the clinical findings in their series was much abbreviated. The kidneys of one of our patients, presenting this clinical syndrome, showed a similar picture. He was carefully followed during the last year of his life; during this time sufficiently numerous clinical and laboratory observations were made to define the clinical picture of this recently recognized syndrome.

CASE REPORT

J. P., a 46-year-old, white, American railroad gateman with a family history of cardiovascular disease and a past history of diabetes mellitus of 4 years' duration, controlled by diet and insulin, entered the hospital on March 7, 1930, complaining of swelling of the legs of 6 months' duration. He was quite well, except for the diabetes, until 6 months before admission, when he noted swelling of the legs, penis, scrotum and face. Two weeks before admission his arms also became swollen. He complained of nocturia once a night; at no time did he experience cough, dyspnea, orthopnea, chest pain or palpitation.

Examination revealed a well-developed and well-nourished man in no distress. The face, scrotum, penis, wrists, arms and legs were edematous. The heart was not enlarged to percussion. There was slight thickening of the peripheral arteries. A small amount of ascites was present. Ophthalmoscopic examination revealed patches of hemorrhage and exudate. The retinal vessels showed tortuosity and arteriovenous nicking. The disks appeared normal. Blood Wassermann, Kahn and Hinton reactions were negative. The basal metabolic rate was –15 and –11 per cent on two occasions. The patient was given a 1200-calorie, salt-poor diabetic diet containing 40 gm. of protein. Fifteen units of insulin were also given daily. One week later the diet was increased to 1600 calories with 60 gm. of protein. On this regime the patient required 15 units of insulin twice daily. Fluids were limited to 1200 cc. daily. The patient received theocin and Salyrgan on several occasions, resulting in a loss of 8 pounds. He was discharged free of edema on March 24 after having lost 26 pounds.

He did only moderately well, and was readmitted to the hospital on April 17 complaining of weakness of the left arm and leg of 24 hours' duration. Examination revealed a slight shifting dullness in the abdomen, a small amount of fluid and a few coarse rales at both lung bases, moderate edema of the legs and weakness of the left arm and leg. The rest of the examination was similar to that on the first admission. Ophthalmoscopic examination revealed several fresh hemorrhages. The disk margins were hazy, although cupping was normal. Phenolsulfonephthalein excretion 2 hours and 10 minutes after the intramuscular injection of 6 mg. of the dye was 10 per cent. The patient showed a gradual return of strength in the left arm and leg. The diabetes was easily controlled with diet and small doses of insulin. Fluids were limited to 1200 cc. daily. The patient's face became puffy during the first week of his stay, but after several weeks all the edema disappeared. He was discharged improved on May 23, 1930, after having lost 10 pounds.

He did rather poorly, progressively becoming worse, until he was readmitted to the hospital on February 26, 1931, for the third and last time, 9 months after his last discharge, complaining of weakness and progressive swelling of the legs. He had been unable to follow his diet and receive insulin injections. The left hemiparesis continued unchanged. Examination revealed marked pallor, generalized peripheral arteriosclerosis, dullness and occasional rales at both lung bases, a small amount of ascites and pitting edema of the hands and legs. Ophthalmoscopic examination showed progression of the retinitis, with an increased amount of exudate and fresh hemorrhages. The diabetes was easily controlled with diet and small doses of insulin. The patient was given a salt-poor diet, and fluids were restricted to 1000 cc. daily. On this regime most of the edema disappeared. However, the blood nonprotein nitrogen rose steadily and the patient became drowsy. Edema of the legs and signs of fluid in the chest developed shortly before death, which occurred on March 27. Bilateral thoracentesis with removal of 1750 cc. of fluid was without avail.

A summary of the laboratory findings of the last year of the patient's life revealed the following. The specific gravity of thirty-nine urines varied between 1.004 and 1.032; one half were over 1.016; during the last month of the illness it fluctuated between 1.008 and 1.018. A trace to a large trace of albumin was present in practically all the specimens. The urinary sugar was 2.5 per cent when the patient was first seen, and showed a tendency to rise between hospital admissions; the sugar disappeared while the patient was under treatment in the hospital. Acetone bodies were found in the urine on one occasion during the beginning of the period of observation. Over half the urinary sediments showed white blood cells, ranging between 1 and 10 per high-power field. Hematuria was noted in a third of the examinations; the number of red blood cells ranged between 1 and 5 per high-power field.

*From the Nephritic Clinic and Pathology Laboratory, Beth Israel Hospital, and the Department of Medicine and the Department of Pathology, Harvard Medical School, Boston.

†Instructor in medicine, Harvard Medical School; associate physician, Beth Israel Hospital, Boston.

§Associate in pathology, Harvard Medical School; pathologist, Beth Israel Hospital.

Hyaline and granular casts were present in practically all the sediments; on one occasion cellular casts were observed. Doubly refractile bodies in the urine were searched for nineteen times and found on seventeen occasions, on five of which large numbers were present. Serum albumin and globulin determinations were performed on fourteen occasions. The serum albumin fluctuated between 3.1 and 4.7 gm. per 100 cc.; most of the values were below 4.0 gm. The serum globulin varied between 1.0 and 2.0 gm.; over half the determinations were below 1.5 gm. The albumin-globulin ratio was never reversed. The blood cholesterol on fourteen occasions fluctuated between 312 and 463 mg. per 100 cc. The blood sugar varied with the control of the diabetic condition; during the uncontrolled periods it rose as high as 488 mg.; in the controlled periods it fluctuated between 72 and 133 mg. per 100 cc. The blood nonprotein nitrogen was normal during the early period of observation, then became slightly elevated, and in the last 6 weeks of the illness was markedly elevated, reaching a level of 117 mg. per 100 cc. terminally. The red-cell count and hemoglobin values showed a steady decline from 4,200,000 and 75 per cent respectively at the beginning of the period of observation to 3,500,000 and 60 per cent shortly before death. The systolic blood pressure varied between 144 and 210, while the diastolic fluctuated between 80 and 110. Shortly before death the blood pressure was 220 systolic, 120 diastolic.

Autopsy. Autopsy was performed 7 hours after death. There was considerable edema of the legs, scrotum and hands. A small amount of fluid was found in the abdominal cavity.

The right kidney weighed 225 gm. and the left 200 gm. Both kidneys were moderately firm and pale grayish-pink. The capsules were somewhat thickened and slightly adherent. The surfaces of the kidneys after stripping the capsules were finely granular. The cut surfaces were pale and grayish-yellow. The markings were well defined. The cortex was well delineated and appeared slightly narrowed, measuring 3 to 5 mm. in thickness. The pelvic fat was normal in amount. The pelves, calices and ureters were normal. Microscopic examination revealed moderate to marked hyalinization and thickening of the media of the arterioles and small arteries of the kidneys. A moderate amount of intimal proliferation with deposit of atheromatous material was also present in the small arteries. There was marked thickening of the intercapillary fibrous tissue of many of the glomeruli (Fig. 1). This was usually concentrated in the center of the glomeruli, with smaller masses of fibrous tissue extending out toward the periphery. In many areas the deposit of this fibrous material was so thick as to suggest amyloid, but this was ruled out by staining several sections with methyl violet and with iodine. Sections stained according to McGregor's[2] technic showed the histological picture more clearly than those stained with eosin and methylene blue. The glomeruli varied a great deal in size; some were of normal diameter, while others were shrunken and exhibited varying degrees of diminished vascularity. Scattered glomeruli were represented by solid masses of fibrous material. In occasional glomeruli the endothelial cells were somewhat swollen, but nowhere was proliferation of these cells or the production of intercapillary fibers noted. The basement membrane was slightly thickened. There was no definite crescent formation in the capsules, although they were frequently thickened. In most instances this thickening was due, at least in part, to the deposition of fibrous tissue. The tubular cells varied in appearance; in some areas they were flattened and atrophic, while in others they were swollen and granular or vacuolated. Many tubules contained granular material and casts. Sections stained with sudan III showed a small amount of orange-stained fat in the endothelial cells of a few scattered glomeruli, a moderate amount in most of Henle's loops and very large amounts in many convoluted tubules. Some of this fat was doubly refractile. The interstitial fibrous tissue was edematous and moderately increased in amount; it contained a small number of irregularly distributed lymphocytes. A few of these cells were filled with fat. The

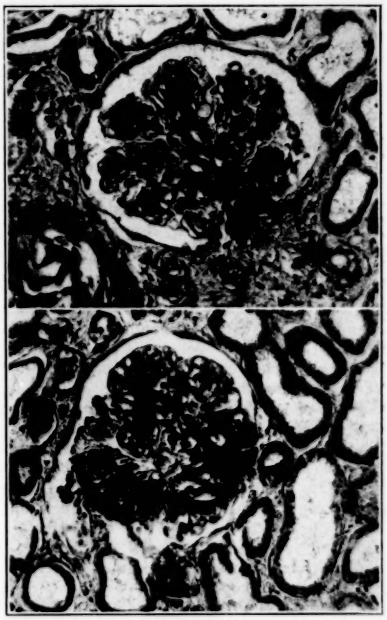

FIGURE 1. *Sections of the Kidney Showing Intercapillary Glomerulosclerosis.*

The upper section was stained with eosin and methylene blue, the lower by the McGregor technic; × 200.

capsules of the kidneys were thickened and contained a few lymphocytes. The renal veins showed no abnormality on gross or microscopic examination.

The heart weighed 360 gm. The coronary arteries showed a moderate amount of atheroma. There was slight hypertrophy of the left ventricle, the wall measuring 2.0 cm. in thickness. Microscopic examination of the heart revealed edema, small areas of fibrosis and slight subintimal hyaline thickening of most of the arterioles. The lungs showed patches of bronchopneumonia. There was a small amount of irregularly distributed fibrosis and fatty infiltration of the pancreas. The arterioles and small arteries of the spleen and pancreas showed moderate to

marked hyaline thickening of the media. Slight hyalinization was observed in the media of the arterioles of the liver, adrenal glands, lymph nodes and skeletal muscle. The aorta exhibited a slight to moderate amount of atheroma. Gross and microscopic examination of the brain was essentially negative except for a moderate amount of atheromatous change in the arteries. The thyroid gland was not remarkable on gross or microscopic examination.

DISCUSSION

The pathological findings in the kidneys of the patient here reported are the same as those described in cases of "intercapillary glomerulosclerosis" by Kimmelstiel and Wilson.[1] The kidneys were large and grayish-pink, and exhibited a considerable degree of arteriosclerosis. The striking renal histological finding was the marked accumulation of intercapillary hyalinized fibrous tissue mainly in the central portions of the glomeruli; the glomerular capsules were also involved. The glomeruli were free of active or healed inflammatory changes such as occur in glomerulonephritis. A considerable degree of fatty change, including the deposition of doubly refractile bodies, was present in the cells of the tubules.

There was a history of diabetes, a recent onset of marked generalized edema, and termination in uremia. Hypertension was found early in the course of the disease. Because of the amount and distribution of the edema and the constant finding of severe albuminuria, Kimmelstiel and Wilson believed that the edema observed in this syndrome is of the nephrotic type. Our patient had profuse albuminuria, hypoproteinemia, generalized edema, hypercholesterolemia, doubly refractile bodies in the urine, a low basal metabolic rate and, early in the course of the illness, normal renal function, all characteristic of the nephrotic syndrome.[2, 4] According to Leiter,[4] the finding of doubly refractile lipoid bodies in the degenerating tubule cells at autopsy strongly favors this diagnosis. All these observations confirm the impression of Kimmelstiel and Wilson that the edema in this syndrome is of the nephrotic type.

Hypertension and evidence of widespread arterial disease, as manifested by peripheral and retinal arteriosclerosis and signs of cerebral vascular accident, were also observed in our patient. The clinical picture was therefore not that of pure lipoid nephrosis but resembled that of the nephrosis seen in glomerulonephritis or renal amyloidosis.

The clinical features of the nephrotic syndrome have been adequately described by many observers.[2, 4] Christian[5] pointed out that this syndrome may occur with a variety of pathologic lesions of the kidney. Cases of the nephrotic syndrome with degenerative lesions of the tubules and glomeruli,[7] renal amyloidosis,[6] glomerulonephritis[8] and, more recently, thrombosis of the renal veins[9, 10] have been described. To these must now be added intercapillary glomerulosclerosis, as defined by Kimmelstiel and Wilson.[1]

The relation of diabetes mellitus to the pathogenesis of this particular renal pathologic change and to the clinical picture is obscure, but that it exists is attested by the fact that all the patients studied by Kimmelstiel and Wilson, as well as the one here described, had diabetes mellitus. Fishberg[11] recently described the nephrotic syndrome in diabetic patients in whom arteriosclerotic and arteriolosclerotic changes were found in the kidneys; glomerular lesions were not, however, included.

This syndrome of diabetes mellitus, hypertension and nephrosis is to be differentiated clinically from congestive heart failure occurring in a diabetic patient by the absence of dyspnea, cyanosis, orthopnea and venous engorgement, and by the presence of generalized rather than dependent edema. Subacute glomerulonephritis with nephrotic edema in a patient with diabetes mellitus cannot be differentiated from this syndrome clinically unless the previous history of acute glomerulonephritis is obtained. The age incidence of glomerulonephritis is quite different from that of the above-described syndrome, but this in itself need not be conclusive in differentiating one from the other. The question naturally arises as to whether the syndrome here discussed is not glomerulonephritis which has been modified clinically and pathologically by moderately severe diabetes mellitus. This question may be answered by the findings in a series of cases which have come to autopsy in our clinic and in which subacute glomerulonephritis with the nephrotic syndrome and diabetes mellitus co-existed; the microscopic renal lesions in these cases were similar in every way to those in patients with subacute glomerulonephritis with the nephrotic syndrome but without diabetes mellitus.

SUMMARY AND CONCLUSIONS

The clinical and pathological findings in a patient presenting the syndrome of diabetes mellitus, hypertension and nephrosis are presented. All the diagnostic criteria of the nephrotic syndrome were noted.

The essential renal pathological findings were identical with those previously described by Kimmelstiel and Wilson, and consisted in sclerosis of the central portions of the glomeruli and the deposition of fatty material, including doubly refractile bodies, in the renal tubular epithelium.

The relation of this type of nephrosis to others is discussed.

A paper entitled "Intercapillary Glomerulosclerosis: A syndrome of diabetes, hypertension and albuminuria," by R. A. Newburger and J. P. Peters has appeared in the December, 1939, issue of the *Archives of Internal Medicine*. The findings of these authors are similar to those recorded here with the exception that there are no studies of the urine by means of polarized light and of the kidneys by means of polarized light and special stains.

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THE EFFECT OF AMPHETAMINE (BENZEDRINE) SULFATE AND PAREDRINE HYDROBROMIDE ON SODIUM AMYTAL NARCOSIS*

ABRAHAM MYERSON, M.D.,† JULIUS LOMAN, M.D.‡ MAX RINKEL, M.D.,§ AND MARK F. LESSES, M.D.§

BOSTON

IN A previous study[1] on the physiologic effects of amphetamine (Benzedrine) sulfate, we noted that the duration of the narcosis produced by the intravenous administration of Sodium Amytal was distinctly shortened if a subcutaneous injection of amphetamine was given either before or after the Sodium Amytal. Since then we have studied the effect of the drug given by the intravenous route which we expected would be even more effective in counteracting the narcotic effects of Sodium Amytal. This paper records the quantitative effects of amphetamine sulfate, as well as Paredrine Hydrobromide, another sympatheticomimetic amine, on the narcosis produced by Sodium Amytal.

MATERIAL AND METHODS

A large number of co-operative, passive patients with dementia praecox were utilized as subjects. An intravenous dose of Sodium Amytal was given to each subject in an amount necessary to produce narcosis of such depth that there was no response to strong stimuli, such as loud noises or face-slapping. At weekly or longer intervals each subject was given a sleep-producing dose of Sodium Amytal followed by amphetamine sulfate,‖ then both drugs simultaneously, and finally amphetamine followed by the narcotic. Intravenous injections of the two drugs were always given, except on rare occasions.

*From the Division of Psychiatric Research, Boston State Hospital, and aided by funds from the Commonwealth of Massachusetts, the Rockefeller Foundation and the Works Progress Administration (Project No. 18088).

†Professor of neurology, Tufts College Medical School; clinical professor of psychiatry, Harvard Medical School; director of research, Boston State Hospital.

‡Assistant professor of neurology, Tufts College Medical School; research associate, Boston State Hospital.

§Research associate, Boston State Hospital.

RESULTS

Administration of Sodium Amytal

Seventeen subjects were given Sodium Amytal alone. It was administered slowly, at the rate of 0.1 gm. per minute. The amount necessary to produce deep sleep varied from 0.5 to 1.0 gm., the average being 0.7 gm.; in some cases the amount varied widely on different occasions. A few subjects who were given the drug several times at three- or four-day intervals required increasing amounts in order to produce deep sleep.

Administration of Sodium Amytal followed by That of Amphetamine Sulfate

In 19 cases deep sleep was produced by Sodium Amytal, immediately after which, or within a few minutes, amphetamine sulfate (30 to 40 mg.) was injected intravenously through the same needle. In 16 cases clear-cut awakening occurred within ten minutes after the injection of the amphetamine. In the other 3 cases it occurred in sixteen, nineteen and twenty minutes respectively. Nine of the subjects awoke within five minutes, at the

‖Benzedrine Sulfate (the trade name of amphetamine sulfate) and Paredrine Hydrobromide were supplied through the courtesy of Smith, Kline and French Laboratories, Philadelphia.

time when the height of the reaction to the amphetamine occurred, as evidenced by the greatest rise in blood pressure, which sometimes reached

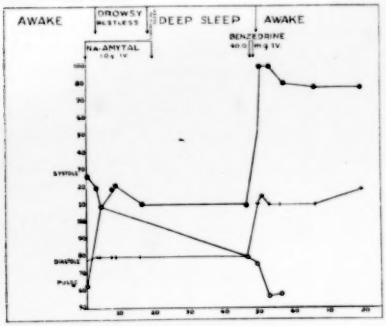

FIGURE 1. *Effect of Sodium Amytal Followed by Amphetamine Sulfate.*

The subject awoke almost immediately after the injection of 40 mg. of amphetamine sulfate.

a level of 200 systolic or higher. As the effect of the amphetamine wore off the subjects appeared to become drowsy. They were, however, able to get off the table and walk about, with some ataxia and complaint of dizziness. Some of them, if allowed to continue lying on the table, tended to fall back into a superficial sleep. They were, however, readily aroused and were able to return to the wards with little or no assistance (Fig. 1).

Simultaneous Administration of Amphetamine Sulfate and Sodium Amytal

In 5 cases the two drugs were administered simultaneously — a total of eleven experiments. The amount of Sodium Amytal given varied between 0.5 and 1.0 gm. The dose of amphetamine sulfate varied in most cases between 20 and 30 mg., administered intravenously, except in 1 case in which 14 mg. was given intramuscularly. The amphetamine was given at the same rate as the Sodium Amytal, so that 1 cc. of the former solution, containing 2 or 3 mg., and 1 cc. of the latter, containing 0.1 gm., were injected simultaneously.

In no case was either superficial or deep sleep produced. Only slight drowsiness was noted. The speech of all the subjects showed thickness and ataxia. Questions, however, were answered coherently. Mild euphoria and talkativeness occurred in 3 cases. All 5 subjects were able to get off the table and dress, although with some ataxia of the legs. The blood pressure in every case except 1 showed the predominating influence of the amphetamine, the rise varying between 26 and 40 mm. of mercury; in the sole exception a fall of 14 mm. occurred. The effect of ampheta-

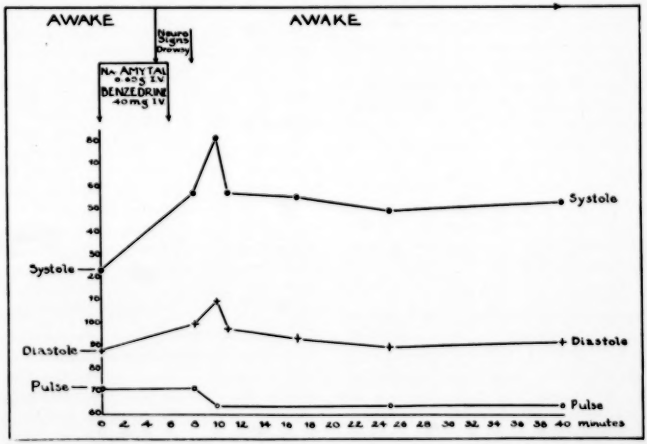

FIGURE 2. *Effect of the Simultaneous Administration of Sodium Amytal and Amphetamine Sulfate. Sleep did not occur during the entire period of observation (1 hour and 40 minutes).*

mine on the pulse rate was predominant over that of Sodium Amytal, so that a fall of 8 to 18 beats per minute occurred, except in 2 cases in which a

rise of 4 and 8 beats respectively was noted (Fig. 2).

Administration of Amphetamine Sulfate Followed by That of Sodium Amytal

In 10 cases the administration of amphetamine sulfate (30 mg. intravenously) was followed by that of Sodium Amytal (0.5 to 1.0 gm.), usually

Neurologic Changes

The well-known neurologic changes[2] which occur during Sodium Amytal narcosis were observed, namely constriction of the pupils, nystagmus and changes in the deep reflexes. In a few cases the knee jerks were difficult to elicit; in the rest they were increased. Ankle clonus was observed in several cases; the Babinski sign was

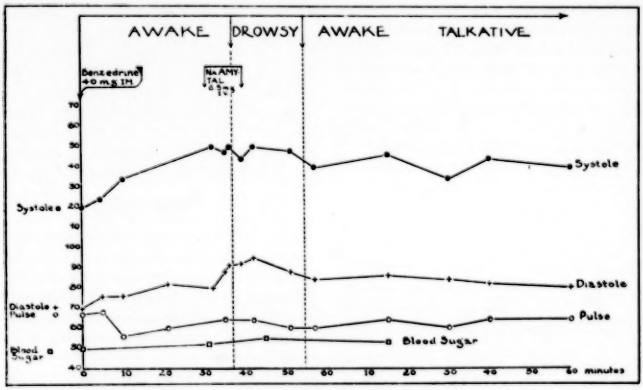

FIGURE 3. *Effect of Amphetamine Sulfate Followed by Sodium Amytal. Sleep did not occur; the subject was drowsy for a short period.*

within fifteen minutes, but occasionally as long as half an hour later. In 4 cases deep sleep lasting from five to twenty minutes occurred, followed by awakening. In the other 6 cases only drowsiness was evident. Five of the latter subjects became very talkative during or after the injection of Sodium Amytal and their accessibility was quite marked. There seemed to be no direct relation in the 10 cases between the change in blood pressure and the awakening, nor did it appear to make any difference in the sleep or awakening whether the Sodium Amytal was given a few minutes or half an hour after the amphetamine. In one case in which the rise in blood pressure following the injection of amphetamine was 60 mm. the patient showed only drowsiness and was very talkative and lively. In another in which the rise was 40 mm. deep sleep lasted for twenty minutes. In both these cases the Sodium Amytal was given within five minutes of the amphetamine. The blood pressure usually fell somewhat following the injection of Sodium Amytal, but never to the original level.

The pulse rate diminished in every case during the administration of amphetamine and returned almost to its original level at the height of the reaction to Sodium Amytal (Fig. 3).

never noted. On the subjects' awaking from the narcosis the pupils returned to their original size. A similar phenomenon was observed when they were awakened with amphetamine sulfate. Nystagmus was invariably observed after 0.2 to 0.4 gm. of Sodium Amytal had been injected, either alone or with amphetamine. The abdominal reflexes always disappeared during the Sodium Amytal narcosis; this was never noted following the giving of amphetamine alone.

When the two drugs were given simultaneously and sleep was prevented, the size of the pupils remained unchanged. Amphetamine by itself had little or no effect on the neurological status. It appeared, however, to enhance the changes caused by Sodium Amytal alone. Thus, the knee jerks became more lively, and in 2 cases ankle clonus was elicited.

Effect of Sodium Amytal and Paredrine Hydrobromide

The chemical make-up of Paredrine (*p*-hydroxy-*a*-methyl-phenylethylamine) is closely related to that of amphetamine, differing from the latter in having added a hydroxyl radical in the para posi-

tion. In animals its action has been shown by Alles[3] to be essentially confined to the peripheral sympathetic nervous system.

A preliminary group of subjects first received Paredrine Hydrobromide intravenously in doses between 10 and 20 mg. A rapid and marked increase in systolic blood pressure occurred, reaching a height of 200 mm. or higher within five minutes, and falling slowly to normal, usually within an hour.

Three subjects were put into deep sleep with Sodium Amytal and then given intravenous injection of Paredrine Hydrobromide. The first subject received 0.65 gm. of Sodium Amytal and 20

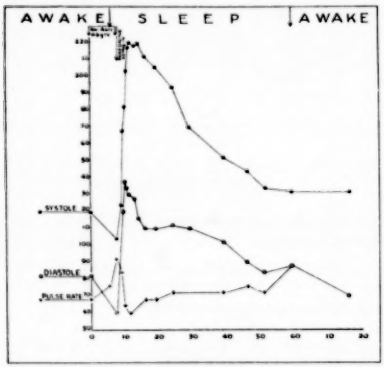

FIGURE 4. *Effect of Paredrine Hydrobromide on the Narcosis Produced by Sodium Amytal.*
The subject remained asleep for fifty-five minutes.

mg. of Paredrine immediately thereafter. He remained in deep sleep for one hour. The blood pressure, which had fallen from 110 systolic, 70 diastolic to 90, 52, after the injection of Sodium Amytal, rose to 196, 20, five minutes after the administration of Paredrine, gradually falling to 116, 82, fifty minutes later. The pulse fell from the original of 88 per minute before and during the narcosis to 56 at the time the blood pressure was at its maximum. It was 64 at the end of the experiment.

The second subject went into deep sleep after receiving 0.5 gm. of Sodium Amytal. A dose of 20 mg. of Paredrine obviously failed to shorten the sleep, which lasted for fifty minutes. The changes in blood pressure and pulse are shown in Figure 4.

The third subject went into deep sleep following the administration of 0.65 gm. of Sodium Amytal. A dose of 10 mg. of Paredrine was then injected intravenously. The narcosis lasted for forty minutes. The blood pressure, which remained essentially unchanged during the administration of Sodium Amytal, rose from 104 systolic, 88 diastolic, to a maximum of 150, 90, five minutes after the injection of Paredrine and returned to 118, 88, forty minutes later. There was no essential change in pulse rate during the experiment.

A fourth subject was given 0.7 gm. of Sodium Amytal and 14 mg. of Paredrine simultaneously by intravenous administration. Superficial sleep resulted. Deep sleep began three minutes later, and it lasted for thirty-eight minutes. The blood pressure rose steadily from 124 systolic, 74 diastolic, to 160, 96, during the administration of the drugs. Ten minutes later it was 128, 80. The pulse rate fell from 80 to 60 at the time when the blood pressure was at its maximum. It was 56 when the blood pressure had returned to its original level.

DISCUSSION

The data here presented indicate that amphetamine sulfate is effective in preventing or counteracting the narcosis produced by Sodium Amytal. The most clear-cut and valid of the experiments were those in which both drugs were given simultaneously. In these cases neither superficial nor deep sleep occurred. Furthermore, sleep usually failed to occur or was markedly shortened when Sodium Amytal followed the amphetamine, and awakening from the Sodium Amytal narcosis occurred quickly after the amphetamine was administered.

In marked contrast to the effects of amphetamine, Paredrine Hydrobromide appeared to have no effect in counteracting the Sodium Amytal narcosis. This corroborates the results obtained by Alles[3] in similar experiments on animals. Unpublished observations on other autonomic functions which we have carried out indicate that Paredrine and amphetamine act similarly on the peripheral nervous system. It is noteworthy that the addition of a hydroxyl radical in the para position of the amphetamine molecule in order to produce Paredrine eliminates its antihypnotic action.

As indicated in a previous study,[1] there appears to be no direct relation between a marked change in blood pressure and the production of sleep, for in the dosage used the increase in blood pressure following the administration of Paredrine is as great as that following the administration of amphetamine. This theory is of course further substantiated by the fact that small doses of amphetamine, which do not affect the blood pressure, interfere with sleep in normal individuals and prevent attacks of narcolepsy.

Whether the effect of amphetamine on Sodium

Amytal narcosis and on sleep is due to a specific involvement of the hypothalamic sleep center or to a widespread cortical stimulation cannot be answered through our experiments. We lean to the belief that these effects are to be accounted for on general cerebral stimulation rather than on any action on a specific center. Thus, not only does amphetamine counteract or prevent sleep, but it affects mood, tends to overcome the feeling of fatigue and has a stimulating effect on psychologic and intellectual processes, as demonstrated by the observations of Peoples and Guttmann[4] and Sargant and Blackburn.[5] The great effectiveness of amphetamine in counteracting the narcosis of Sodium Amytal probably lies in its widespread action on the brain, in which it resembles Sodium Amytal itself, which is recoverable from practically all parts of the brain.[6]

It is unlikely that amphetamine chemically neutralizes Sodium Amytal; it is more probable that it stimulates those areas which have already been released from normal inhibitory control by Sodium Amytal. Sodium Amytal may be considered to release from normal inhibitory control not only the emotions but also reflex action. Thus, not only do such emotional changes as overtalkativeness, a state of euphoria and other signs of intoxication result from its administration, but there are usually present nystagmus, an increase in deep reflexes, with the occasional presence of ankle clonus, and the constant suppression of the abdominal reflexes. The addition of amphetamine not only counteracts the narcosis, but also appears to enhance some of the neurologic effects of Sodium Amytal.

Summary and Conclusions

Amphetamine (Benzedrine) sulfate is effective in preventing or counteracting the narcosis produced by the intravenous administration of Sodium Amytal. This action and the fact that amphetamine causes a rapid and prolonged rise in blood pressure may be found useful in certain medical or surgical cases in which it seems desirable to overcome severe side reactions of the narcosis produced by the barbiturates, particularly respiratory embarrassment and pronounced decrease in blood pressure.

Paredrine Hydrobromide, although closely related to amphetamine, appears to have no effect on the narcosis produced by Sodium Amytal.

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THE CHEMICAL AND CLINICAL DIAGNOSIS OF ACUTE ALCOHOLISM*

Walter W. Jetter, M.D.†

Taunton, Massachusetts

THE various phases of the problem of alcoholism, particularly the diagnosis of acute alcoholic intoxication, have assumed great importance in recent years. This is undoubtedly the result of attempts throughout the country to decrease the number of traffic accidents. The advent and increased use of the chemical method for the determination of alcohol in various body tissues have introduced a new weapon for the study of the problem. Because of the comparatively recent origin and potential medicolegal importance of the chemical test for alcohol, it has been thought that a brief résumé of the various principles involved in the diagnosis of acute alcoholism by this method, together with an account of personal experience in its use, might be pertinent.

*From the Department of Pathology, Taunton State Hospital, Taunton, Massachusetts.

†Pathologist, Taunton State Hospital.

Pharmacology of Alcohol

The pharmacologic action of alcohol is that of a depressant, particularly on the central nervous system. With small doses it is an "inhibitor of inhibitions," with the consequent feeling of well-being, relaxation and so forth, but is detrimental to accuracy of attention and judgment. With larger doses the depressant action is more noticeable and there is greater disturbance of the emotions. Some individuals become excited and noisy or melancholy and sad; others exhibit a fighting mood, while still others become drowsy. At the same time there is marked impairment of the muscular activities. With still larger doses stupor and coma may result.

As alcohol is absorbed rapidly from the small intestine, and to a limited extent from the stomach, its maximum concentration in the blood is

usually reached one or two hours after the ingestion of an alcoholic beverage. Various factors, such as the amount of alcohol consumed, the alcoholic concentration of the beverage and the presence and type of food in the gastrointestinal tract, influence the rate of absorption. The diffusion of alcohol throughout the body tissues, with the exception of adipose tissue, occurs uniformly and rapidly, although there is a skeletal-muscle lag lasting from three to four hours, as shown by Harger, Hulpieu and Lamb[1] in experimental animals. In general, however, the concentration of alcohol in the blood represents that in other body tissues, including the brain. Oxidation occurs at a uniform rate (4 to 15 cc. per hr. on basis of 70 kilograms of body weight), probably regardless of the amount of alcohol in the body.[2] Excretion is effected by two chief routes, the lungs and the kidneys, and is complete within twenty-four hours after ingestion.

CHEMICAL ANALYSIS FOR THE DETERMINATION OF ALCOHOL

Various methods are available for the determination of alcohol in body tissues, including the blood, urine, saliva and expired air.[3–8] Most of these methods are dependent on the ability of alcohol to be easily oxidized in acid solution. I have had considerable experience with two methods,[3, 4] both of which are applicable to blood and urine analyses.

In Heise's[3] method, the proteins are precipitated by a tartaric-picric acid solution. Distillation is carried out directly, without preliminary removal of protein. The alcohol contained in aliquot portions of the distillate is oxidized by potassium dichromate in sulfuric acid on a boiling-water bath. The concentration of alcohol is determined by direct comparison with known standards carried through the same procedure. This method is sufficiently accurate for clinical use and is time-saving, since many samples may be run simultaneously.

In Harger's[4] method, which is also applicable to the analysis of tissues, preliminary precipitation and filtration of the proteins are necessary. The protein-free filtrate is distilled and the alcohol in aliquot samples is oxidized by standard potassium dichromate solution, positive heat of solution being obtained by the addition of concentrated sulfuric acid. Excess dichromate is determined by titration with a reducing fluid of methyl orange and ferrous sulfate. This method is more accurate than that of Heise, and by proper dilution of the reagents the so-called normal alcohol content of the fasting individual may be determined. In approximately 125 normal cases I[9] have had results varying from 0.007 to 0.004 gm. per 100 cc. (0.007 to 0.004 per cent) blood alcohol.

The alcohol in the saliva may be determined by a method devised by Friedman,[5] and in the expired air by the method of Harger, Lamb and Hulpieu.[6]*

SPECIFICITY OF THE TEST

Any volatile reducing substance interferes with the determination, but in the normal individual no such substances are present. Acetone bodies are reducing, but may be detected qualitatively and removed quantitatively. In a series of cases with ++++ acetone tests in the urine, the concentration in terms of alcohol was only 0.04 gm. per 100 cc. in both blood and urine, hardly enough to have an appreciable effect on clinical interpretation.[10] Methyl alcohol has reducing properties, but may be detected in the filtrate by oxidizing it to formaldehyde and testing qualitatively for this substance. Also, the urine should be tested for formaldehyde if the subject has been receiving urotropine, since formaldehyde, a volatile reducing agent, may be produced in the kidneys. Other substances such as paraldehyde, ether, the barbiturate derivatives and acetanilid have no interfering action.

COLLECTION OF SAMPLES

In the collection of samples of blood, the arm should be sterilized with a mercuric chloride solution and wiped dry with sterile cotton. Care should be taken that no contact is made with alcohol. The best preservative is sodium fluoride, since, as Heise[3] has shown, the alcohol content of blood does not deteriorate appreciably in thirty days if preserved by this substance. Addition of benzoic acid preserves the alcohol in urine indefinitely. Samples should be taken, labeled and sealed in the presence of witnesses if the case is of medicolegal significance.

CORRELATION OF CHEMICAL DATA AND ACUTE ALCOHOLIC INTOXICATION

For a correlation between chemical data and acute alcoholic intoxication, it is necessary to have some clinical criteria for the diagnosis of the condition. In a series of 1165 cases admitted to the Edward J. Meyer Memorial (Buffalo City) Hospital with a diagnosis of acute alcoholic intoxication, I[10] used the following physical criteria as diagnostic.

(1) The subject must exhibit an abnormality of gait, that is staggering, swaying, reeling and so forth. If he was

*The method for determination of alcohol in the expired air is advantageous because a sample may be taken without the physical and legal difficulties encountered in taking a blood specimen. Also, a result may be obtained within a few minutes. Its disadvantages are that the apparatus is somewhat cumbersome, and that sufficient data have not been accumulated correlating the amounts of alcohol in the expired air and in the blood.

in coma, a follow-up study on the wards was considered essential for an accurate conclusion.

(2) The subject must exhibit two of the following four criteria:

a. Abnormality of speech, as shown by slurring or incoherence. Trick phrases difficult to pronounce were not used; instead, the subject was asked only familiar questions, such as inquiries as to name, residence, age and so forth.

b. Dilatation of the pupils.

c. Flushing of the skin.

d. Alcoholic odor in the breath.

It will be realized that dilatation of the pupils and flushing of the skin are not necessarily characteristic of alcoholic intoxication. Although produced by drinking, they are also found in numerous other conditions. Even an alcoholic odor, supposedly easy to recognize, is sometimes mistaken for some other odor; in a number of cases it was thought to be present but a test for blood alcohol was negative. Abnormalities of gait and speech, while characteristic of intoxication, may also be produced by other conditions. It was assumed, however, that if these criteria were present in the proper sequence, that is, abnormality of gait and in addition two of the other four criteria, — speech abnormality, dilated pupils, flushed skin and alcoholic odor, — the clinical diagnosis of acute alcoholic intoxication was justified.

Criticism has been attached to this definition of acute intoxication on the ground that it tends to eliminate all cases but those grossly intoxicated. While this is admitted, it is believed that the criteria are easy of detection, and could be adhered to uniformly throughout a given series of cases. Furthermore, their value lies in the fact that they comprise a definite standard for the clinical diagnosis of acute alcoholism, in place of the vague term "under the influence of alcohol."* The clinical interpretation of the latter would undoubtedly vary with the examiner, and it is much more difficult to adhere to without variation in a large series of cases than are our criteria, which are easy of recognition and interpretation.

Using these criteria for the clinical diagnosis of acute intoxication in a series of 1000 cases with alcohol in the blood,[10] the diagnosis was made in 47 per cent of the cases with a concentration of 0.15 gm. per 100 cc., as shown in Table 1 and Figure 1. The incidence was 83 per cent at a concentration of 0.20 gm. per 100 cc., and rose to 90 per cent at 0.25 gm. A total of 638 of the 1000 cases were found at these three concentrations. At levels exceeding 0.25 gm. per 100 cc., acute intoxication gradually approached an incidence of 100 per cent, which condition was reached at 0.45 gm. of blood alcohol. Intoxication was usually severe at these higher concentrations, and coma was not uncommon when the blood alcohol was as high or higher than 0.35 gm. The two deaths attributed to acute alcoholism, with blood alcohol levels at 0.47 and 0.48 gm. respectively, were confirmed by autopsy. No cases were encountered having a concentration of over 0.50 gm. In another series of over 800 cases,[9] 1 showed a concentration above this level, namely 0.74 gm. This patient died of acute alcoholism.

TABLE 1. *Number and Percentage of Cases of Acute Intoxication at Varying Levels of Blood Alcohol Concentration (1000 Cases).*

Blood Alcohol Concentration	No. of Cases	Clinical Diagnosis of Acute Intoxication	
		No. of cases	Per cent
gm. per 100 cc.			
0.05	38	4	10.5
0.10	87	16	18.4
0.15	132	61	47.0
0.20	330	276	83.6
0.25	176	158	90.0
0.30	141	133	95.1
0.35	74	71	96.0
0.40	15	14	93.3
0.45	5	5	100.0
0.50	2	2	100.0
Totals	1000	740	

A consideration of similar data obtained by other workers, namely Hoffman,[12] Widmark[13] and Schwarz[14] in Europe and Bogen[15] and Harger, Lamb and Hulpieu[6] in this country, demonstrated somewhat similar results, that is a rise in the incidence of acute intoxication at blood alcohol concentrations from 0.10 to 0.20 gm. per 100 cc.

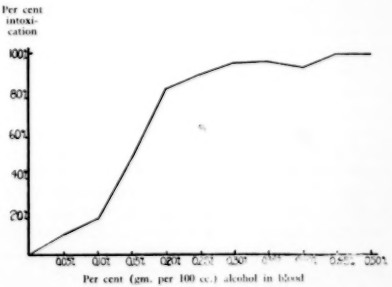

FIGURE 1. *Percentage Occurrence of Clinical Intoxication at Various Concentrations of Alcohol (1000 Cases). Reproduced by courtesy of* American Journal of the Medical Sciences *(196:480, 1938).*

*The Supreme Court of Arizona[11] has defined this condition as follows: "The expression 'under the influence' of intoxicating liquor covers not only the well-known and easily recognized conditions and degrees of intoxication, but any abnormal mental or physical condition which is the result of indulging in any degree in intoxicating liquors, and which tends to deprive him [the imbiber] of that clearness of intellect and control of himself which he would otherwise possess. . . ."

However, an incidence of 100 per cent was noted at a blood alcohol concentration of 0.20 to 0.25 gm. per 100 cc., whereas in the present series all individuals were not intoxicated until a level of 0.45 gm. had been reached.

Such a variation as that just noted is not easy to explain. It may be due in part to differences in the criteria for evaluating acute intoxication, for in none of the series previously mentioned were the criteria clearly defined. It is also believed that individual tolerance is a potent cause of this variation. For example, several subjects, all chronic drinkers, were examined and found relatively sober by all clinical tests, yet the blood alcohol concentration varied from 0.35 to 0.45 gm. per 100 cc. It should be emphasized that this is a concentration close to the lethal point, and one at which severe intoxication or even coma is the common finding. That such a tolerance is not based on variability in the absorption of alcohol seems clear, since it is only the actual concentration of alcohol in the blood that is considered, and not the amount of alcohol ingested. This series, as might be expected in any large group of cases of acute alcoholism, was composed largely of chronic cases, that is, persons in the habit of consuming some sort of alcoholic drink in appreciable quantities as a daily routine. Since it is believed that tolerance to alcohol can be acquired, this factor may be expected to account for the variation in the incidence of intoxication in our series as compared with that in those previously mentioned.

This is clearly illustrated by experimental work in which a volunteer group, consisting of alcoholic neophytes or occasional drinkers, were fed alcohol.[16] These subjects were examined for acute alcoholic intoxication by the same clinical criteria as those used in the larger series. All were clinically intoxicated at a blood alcohol concentration of 0.20 gm. per 100 cc., as compared with the incidence of 83 per cent at the same concentration in the larger group, consisting primarily of chronic drinkers. In addition, it appeared that the occasional drinker exhibited a slight tolerance in comparison to the neophyte. Whether this tolerance, shown to the highest degree in the chronic alcoholic patient, is produced by an altered blood-brain alcohol ratio is unknown. Nevertheless, it would seem that some unknown mechanism exists in this type of individual protecting him from the severe clinical manifestations of acute alcoholism commonly found in the average person at these high blood alcohol concentrations.

ADVANTAGES OF THE CHEMICAL DETERMINATION OF ALCOHOL

In cases of coma, chemical determination of the alcohol content of the blood or urine should be as routine a procedure as are analyses for urea and sugar. For example, in 37 comatose patients referred to the Edward J. Meyer Memorial Hospital as cases of alcoholism, the diagnosis was proved erroneous by a negative blood alcohol test.[10] As shown in Table 2, coma was produced in 16

TABLE 2. *Correct Diagnoses in 37 Alcohol-Free Cases with a Preadmission Diagnosis of Acute Alcoholic Coma.*

DIAGNOSIS	NO. OF CASES
Barbital poisoning	8
Paraldehyde poisoning	8
Fractured skull	7
Cardiovascular accident	5
Schizophrenia	2
Diabetes mellitus	2
Uremia	2
Psychosis	1
Epilepsy	1
Central-nervous-system syphilis	1
Total	37

cases from overdosage with either paraldehyde or barbital derivatives, while diabetes mellitus, uremia, cerebral injuries, cardiovascular accidents and schizophrenia were also found.

On the other hand, the possibility of the coma's being produced by alcohol must also be considered. For example, the police requested the admission of a man found lying unconscious in the street. After artificial respiration had been administered by firemen, the patient was brought to the hospital with a diagnosis of heat stroke. On admission the possibility of alcoholic coma was suspected. The alcoholic concentration of the blood was 0.37 gm. per 100 cc. Thus the determination of the concentration of the alcohol in the blood or urine is of definite value in the differential diagnosis of coma.

It is in the medicolegal field that the chemical method should prove of greatest value, particularly in automobile accidents. First of all, it determines accurately whether an individual has been drinking. Second, from the determined concentration of the blood alcohol it is possible to estimate the approximate amount of alcohol ingested, provided that the drinking has occurred within an hour or less.[16] It should be emphasized that the sample of blood required for analysis should be taken as soon as possible after apprehension, preferably within an hour. However, if the sample is not obtained within this time, the level of alcohol at the time of apprehension may still be estimated by an interpretation of the curve showing the relation

between the elapsed time after drinking and the concentration of alcohol in the blood.[16]

The actual blood alcohol concentration at which a person should be considered intoxicated would seem to depend on the definition one uses in diagnosing the condition. In automobile accidents, the leading cause for the arrest of alcoholic individuals, the complete syndrome of clinical intoxication, with its gross staggering, reeling, incoherence or coma, should apparently not be adopted. Actually a person at this stage of intoxication may be physically unable to drive a car, and usually does not do so. Furthermore, of a number of persons who are drinking probably only a small percentage consume enough of an alcoholic beverage to place them in this category. Nevertheless, it is these individuals who, even though not intoxicated according to our criteria, may become a menace at the wheel of an automobile.

Numerous experimental data have been accumulated tending to prove that even small concentrations of alcohol in the blood (0.04 to 0.10 gm. per 100 cc.) slow the reaction time, impair judgment, increase the number of errors while performing mechanical tests and so forth. Bauer[17] has published a report of his work showing that the presence of alcohol in experimental subjects increased the speed at which they drove their automobiles. Heise and Halporn[18] have shown in actual road tests that an individual with a blood alcohol concentration of 0.10 gm. per 100 cc., induced by the administration of 5 ounces of whisky in a short period of time, requires 50 per cent more distance to brake his car to a stop on signal than does the same individual when alcohol free. That drivers who have been drinking are more liable to be involved in accidents has been shown by Holcomb.[19] He noted that 47 per cent of drivers so involved had appreciable amounts of alcohol in the blood, in comparison with only 12 per cent of a group of drivers picked at random who were not involved in accidents. Also, the average person with a blood alcohol concentration of 0.15 gm. per 100 cc. was fifty-five times more likely to have an accident than a driver with no alcohol in his blood. Thus it would appear that the complete syndrome of acute intoxication is unnecessary in order to make the diagnosis in automobile-accident cases. Hence the term "under the influence" acquires significance.

The National Safety Council[20] has adopted an alcohol concentration of 0.15 gm. per 100 cc. in the blood or 0.20 gm. in the urine* as inconsistent with the safe operation of a motor vehicle, and a level at which prosecution should be conducted in automobile accidents and traffic violations. This seems logical, although it should be emphasized that even lower concentrations of blood alcohol, down to 0.10 gm. per 100 cc., may be of significance in all cases except those in which tolerance has been developed to a high degree. While only 50 per cent of cases in a group of habitual drinkers will be clinically intoxicated at a blood alcohol level of 0.15 gm. per 100 cc., sufficient impairment of faculties will be present in even this type of individual to make him a menace as a driver. However, it should be remembered that this type of drinker forms only a small portion of the general population, and because of his alcoholic tendencies is likely to be of so low an economic status as to eliminate him from the car-owner and driver class. It is rather the alcohol neophytes and the occasional drinkers with a relatively low tolerance who form by far the largest group involved in motor accidents. In any case, a blood alcohol concentration of 0.15 gm. per 100 cc. represents an appreciable consumption of an alcoholic beverage, as the average person weighing 70 kilograms must ingest 6 or 7 ounces of 100-proof whisky within an hour in order to attain this level.[16]

* * *

The value of the chemical method in the detection of intoxication is evident. The difficulties of proving satisfactorily to a court and jury at some later date that a given individual was "under the influence" on clinical findings alone are notorious. While the defendant seldom contends that he has had nothing to drink, he usually has witnesses who testify that he was thoroughly sober at the time of arrest and had taken only a small quantity of liquor, for example one glass of beer. Furthermore, the shock of an accident, the sobering effect of the arrest and the apprehension felt while awaiting trial may so affect the defendant as to cause doubt in the examiner's own mind as to the part that alcohol played in the accident. The chemical test would do much to clear up these difficulties, both in a positive and a negative sense, since it shows whether the individual has been drinking and, more important, the approximate amount of liquor that must have been consumed.

The value of the chemical determination of alcohol in the blood and urine lies in the fact that it is an added weapon in the diagnosis of inebriation; but it should be supplemented whenever possible by such physical data as can be collected by a competent observer. It should not be assumed that the chemical method makes clinical evaluation obsolete; rather it should be considered an-

*In a series of 372 cases in which simultaneous examinations of the blood and urine alcohol were performed, the ratio of blood alcohol to urine alcohol was 1:1.32.[21] At the higher concentrations of alcohol the ratio tended to approach unity, whereas at low concentrations it varied considerably. A fair assumption could be made from this work, however, that an alcohol concentration of 0.20 gm. per 100 cc. in the urine represents at least 0.15 gm. in the blood.

other means of arriving at a proper interpretation of certain physical and mental abnormalities which may or may not have been produced by alcohol. A combination of the chemical and the physical examinations should offer a better chance for the detection and conviction of the inebriated than is afforded by either method alone. It is to be hoped that legislation will be passed which requires the addition of the chemical method in the diagnosis of suspected alcoholic intoxication.

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REPORT ON MEDICAL PROGRESS

CURRENT EPIDEMIOLOGICAL ASPECTS OF SCARLET FEVER*

JOHN E. GORDON, M.D.†

BOSTON

SCARLET fever today is just about as prevalent as it ever was. The general level of severity, however, has progressively decreased over a long period of years. Experienced clinicians recognize these facts, and they are substantiated by the prevailing low case fatality and mortality rates in the world at large. The fewer deaths from scarlet fever that occur now as compared with a half century ago are related but little to improved methods for prevention and control. A good deal of this change is due to a better level of general health conditions, a factor difficult to measure but undoubtedly real. Better methods of medical management for those who become ill have contributed materially to the lower case fatality. Probably the most important influence is the existing favorable state of equilibrium between host and parasite. How much of the latter is dependent on greater community resistance from increased numbers of inapparent and atypical infections, and how much is directly concerned with altered biologic activities of the infectious agent that have presumably taken place in the past sixty years, is difficult to determine. Neither is it possible to venture much of an opinion as to how stable is the present equilibrium or how permanent it may be. There is need for better definition and explanation of the epidemiological relations involved in the behavior of this disease, if improved control measures are to be developed that may lead to as favorable an influence on incidence as has occurred in respect to deaths.

Our conception of scarlet fever as a disease has undergone material change in the past several years. This started with the contributions of Dick and Dick[1] and of Dochez[2, 3] in 1924, which served to reopen the whole question of the part that streptococci have in the causation of scarlet fever. These studies, and the many that followed shortly thereafter, resulted in almost universal agreement that the infectious agent responsible for the disease belongs to the group of hemolytic streptococci. The extensive laboratory investigations since then have had the usual effect of a better appreciation of epidemiological problems that ordinarily comes from greater knowledge of the infectious agent.

The principal epidemiological advances have come from application to field investigations of

*From the Department of Preventive Medicine and Epidemiology, Harvard Medical School, Boston.

†Professor of preventive medicine and epidemiology, Harvard Medical School; consulting physician, Haynes Memorial Hospital, Boston.

newly developed laboratory methods for the study of hemolytic streptococci. These studies have been concerned not only with scarlet fever itself but with other clinical conditions caused by this infectious agent. Interrelations have been defined that have led to an interpretation of scarlet fever as being but one of the multiple manifestations of hemolytic streptococcus infection in man, distinguished from the others by the addition of toxic manifestations to the ordinary reactions of tissue invasion that characterize streptococcal disease in general (Okell[4] and Griffith[5]). What has long been considered a specific infectious disease, in the sense of cholera and plague, now appears to be a disease syndrome caused by any one of a wide variety of hemolytic streptococci. The factors that determine whether scarlet fever or simple streptococcal infection is to develop are two individual and variable characteristics, one related to the host and the other to the parasite. That of the infectious agent is the capacity to produce erythrogenic toxin; that of the host, the presence or absence of specific resistance to this toxin.

Several kinds of evidence may well be examined in order to determine how well this conception is justified. Is it in agreement with our clinical knowledge of scarlet fever? Does it coincide with observed information about hemolytic streptococci in scarlet fever and in other diseases? And is it compatible with the epidemiologic behavior of the disease?

CLINICAL NATURE OF SCARLET FEVER

Some communicable diseases occur almost invariably as a frank, well-marked attack, presenting classical manifestations wholly typical of that disease. Others show extreme differences in clinical reaction, sometimes seeming to shade off almost unendingly to present such slight host-parasite reactions that the effect is beyond clinical observation, and becomes latent or subclinical infection. Scarlet fever has always been known for its erratic behavior. Erasmus Darwin described the disease as being anything from a fleabite to the plague. Critical examination of even the most extreme clinical forms of scarlet fever gives indication of a syndrome having two components. Certain signs and symptoms can be related to the effects of a toxin; others depend on the septic, infectious or invasive properties of the agent (Cooke[6]). Both can be recognized in varying degree in all forms of classic scarlet fever, the common clinical classification of the disease being largely based on the differences in proportion of toxic and septic elements. Thus, a clinical type exists in which the manifestations are essentially toxic, still another in which septic influences predominate, and a third mixed form which is the usual manifestation of outspoken scarlet fever, and is variously designated as mild, moderate or moderately severe. Aside from this group of readily recognized reactions, there is a group of atypical infections of varying extent, mild in nature and difficult to diagnose. They represent essentially low-grade invasive reactions with the toxic element indefinite and sometimes so slight that the eruption of the skin is most fleeting. The third general form of infection is latent or subclinical. The toxic element is absent and the invasive factor so slightly active that it leads to no clinically recognizable signs. There is clear-cut evidence of the existence of this group, but little appreciation of the number of cases involved in proportion to the other two.

The septic component of the scarlet fever syndrome is present in all recognizable infections. The signs and symptoms result from invasion of tissue, and are like those of all other streptococcal disease, being essentially the same whether the part involved be the pharynx and tonsils as in scarlet fever, the skin as in erysipelas, skeletal muscle as in wound infections or the mucous membranes as in puerperal fever or simple angina. There is malaise, fever, leukocytosis and the reaction of inflammation from lesions in local tissue. There is a tendency to spread by extension to neighboring structures — to the endometrium in puerperal fever, to the middle ear and lymph nodes in scarlet fever and to the lymphatics after surgical infections. The complications of scarlet fever, so outstanding a feature of the disease, are strictly a part of the septic component, and mark an ability of the streptococcus to multiply locally and to invade tissue.

The toxic component of scarlet fever is related principally to constitutional effects, in contrast to the local disturbances resulting from septic action. It is responsible for the exanthem and the enanthem and for the constitutional reactions marked by vomiting, generalized lymphadenopathy, arthralgia and albuminuria.

Together these two components constitute the syndrome scarlet fever. Considering scarlet fever generally, their relative emphasis varies greatly. In the individual case, the preponderance of one component over the other depends on two variants. The first is the relative ability of the streptococcus concerned to form a soluble erythrogenic toxin. The other is the degree of specific resistance possessed by the host, as determined by the content of streptococcal antitoxin in the blood. Thus, infection with a streptococcus that produces erythrogenic toxin can lead to two kinds of clinical reaction. The result in a Dick-negative subject — a

host with antitoxic immunity — is a local infection, corresponding to sore throat or tonsillitis. A Dick-positive subject, lacking antitoxic immunity, develops the complete syndrome of scarlet fever. Infection with a streptococcus unable to generate rash-producing toxin gives only a localized throat infection, irrespective of whether the host has antitoxic immunity or not. It follows, then, that the rash in scarlet fever infection is a fortuitous circumstance, depending on the coincidence of two variable factors, and that scarlet fever differs only from other streptococcal infections in that a toxic element is added to the signs and symptoms of septic infection which characterize all disease due to these micro-organisms. The presence of toxic symptoms is essential to the clinical recognition of scarlet fever infection; its absence does not eliminate that possibility.

The relative importance of these two components from the standpoint of resulting death and disability is of practical significance. Logically a combination of the two should lead to a more serious effect than the presence of one alone. Furthermore, it is conceivable that toxic effect may favor invasion, although precise evidence of any significant relation is lacking. It is well known, however, that most deaths from scarlet fever, as it currently exists, are the result of complications and but little related to acute toxic action. The frequency and extent of complications depend largely on the ability of the micro-organism to invade tissue. Detailed studies of the frequency of complications in streptococcal infections, with and without toxic manifestations, seem to indicate little actual difference. Stebbins, Ingraham and Reed,[7] in their study of mixed epidemics from milk-borne infection, found complications essentially as frequent in persons who had no rash as among those who did. Hobson's[8] observations in England led him to the conclusion that complications were even more frequent when rash was absent than when it was present.

The mechanism of resistance on which recovery from scarlet fever depends is apparently of a dual nature. The ability to prevent growth and progressive invasion of tissue depends on antibacterial protection. Neutralization of toxin is a function of antitoxic resistance. That one type of reaction may have some influence on the other — a high degree of antitoxic immunity contributing to protection against tissue invasion — seems possible, although it is not clear to what extent or in what manner (Maxcy[9]). The unusual cases in which Dick-negative nurses and physicians have had repeated and long-continued exposure before contracting scarlet fever suggests the opposite situation — of resistance to infection without antitoxic immunity — and that the resistance is local and not dependent on circulating antibodies, at least not on antitoxin.

SCARLET FEVER AND OTHER HEMOLYTIC STREPTOCOCCUS DISEASES

Recovery from even the mildest forms of scarlet fever almost invariably gives protection against a second similar attack, combining infection with toxic manifestations. The likelihood of a subsequent angina from infection with a strain of hemolytic streptococcus capable of producing the syndrome with rash in a susceptible host is by no means eliminated. Naturally acquired antitoxic immunity is usually permanent, but the resistance to invasion of tissues is decidedly temporary.

Clinical and epidemiological records of cases of scarlet fever contain repeated indications that streptococci recovered from them cause other kinds of infectious disease. Factual evidence came from the studies of Stevens and Dochez.[10] Field studies in Detroit (Gordon et al.[11]) showed a well-marked frequency of coincident sore throat or upper respiratory infection among family contacts of patients with classic scarlet fever. Remarkably similar results were reported by Ramsey[12] from comprehensive studies in New York State.

Immunologically identical strains of hemolytic streptococci have been repeatedly isolated from the members of a family having angina, some with and some without skin eruption. Other field studies have shown the probable introduction of scarlet fever into families by a member who first developed simple angina, since the hemolytic streptococci from both infections were serologically identical, were usually of a type uncommonly encountered in sporadic sore throat, and sometimes had previously been unrecognized in that community.

One of the best illustrations of the epidemiological relation of scarlet fever to other streptococcal infections of the upper respiratory tract is that reported by Stebbins, Ingraham and Reed.[7] In milk-borne outbreaks of hemolytic streptococcus infection, some persons contracted classic scarlet fever, others developed simple angina, and sometimes there was erysipelas. The relative proportion of hemolytic streptococcus infections with and without toxic manifestations varied from epidemic to epidemic, but both were represented in a given outbreak. In the Wellsville outbreak, for example, 65 per cent of 196 patients had no eruption of the skin, and this was the only essential difference in respect to all patients. The degree of fever and the proportion of complica-

tions were about the same in those both with and without rash. Infections were essentially as frequent among persons with a history of scarlet fever as among those without. Dick tests made after the epidemic had subsided showed the percentage of those reacting negatively to be somewhat greater if the illness had presented the symptoms of scarlet fever than if the clinical manifestations were those of septic sore throat. McLean,[13] in Canada, reports a mixed outbreak of scarlet fever, epidemic sore throat and tonsillitis, wherein tonsillitis and scarlet fever were commoner among children, and septic sore throat among adults.

Another kind of evidence lends strong support to the experience gained from the study of outbreaks and from the reactions of family contacts. By the time adult life is attained, about four of every five persons have become Dick-negative (Zingher[14]), with relatively few having an intervening history of a rash characteristic of scarlet fever. This suggests that infections with toxicogenic streptococci that lack rash are much more frequent than those having this toxic manifestation.

This clinical and epidemiological evidence naturally brings to the private practitioner in medicine the important question as to what interpretation is to be made of streptococcal angina without rash, and what procedure is indicated in respect to family contacts and the protection of the public health. It should be apparent that both patients with angina and rash and those who develop only angina from contact or association with them should be considered as having scarlet fever infection. Both infections are probably due to strains of hemolytic streptococci capable of causing the usual scarlet fever syndrome.

The sporadic case of streptococcal angina or tonsillitis, under present circumstances, is interpreted as an ordinary streptococcal infection. The laboratory methods currently available for determining whether or not the particular strain produces an erythrogenic toxin are too complicated for clinical application. Such an interpretation rests on necessity, with full realization that such sporadic infections are sometimes more than simple angina due to a non-toxicogenic streptococcus. and that the organism concerned may produce scarlet fever if transmitted to a susceptible person. When sore throat occurs in epidemic proportions, some cases of recognizable scarlet fever are certain to occur if the infectious agent is toxicogenic.

It is important to realize that recognition of scarlet fever infection many times depends as much on epidemiological as on clinical methods of diagnosis. Improved results in control are scarcely possible until equal attention is devoted to hemolytic streptococcus infections etiologically identical but clinically divergent.

DIFFERENTIATION OF HEMOLYTIC STREPTOCOCCI

Only those strains of streptococci that are hemolytic and produce erythrogenic toxin are concerned in scarlet fever. Not long after the description of this toxin by Dick and Dick,[15] it became apparent that hemolytic streptococci from a number of other conditions, notably erysipelas (Birkhaug[16]), could produce a soluble toxin, and that this was not a characteristic limited to strains isolated from scarlet fever patients. Long-continued investigations by a number of workers in different countries (Kirkbride and Wheeler,[17] Eagles,[18] Smith,[19] McLachlan[20] and Fraser[21]) brought out other relations. Not infrequently strains producing strong erythrogenic toxin were isolated from conditions entirely apart from scarlet fever. It was learned, furthermore, that strains from scarlet fever varied greatly in the amount or strength of the toxin they could form, although as a rule hemolytic streptococci from non-scarlatinal sources produced weaker toxins than did those from scarlet fever. The most important demonstration, however, was that most erythrogenic toxins, whatever their source, could be neutralized by a single antitoxin obtained from animals injected with the well-known strain—NY 5 (Fraser[21]). If two other antitoxins were used almost all known toxin-producing strains could be separated into one of three groups: a principal group including about 85 per cent of the strains, and two minor divisions. This work brought out that it is impossible either qualitatively or quantitatively to mark off toxicogenic strains obtained from cases of scarlet fever from those found in other conditions.

Much effort has been given to other possible methods for differentiating the hemolytic streptococci which are responsible for the disease, scarlet fever. Important progress was made when Lancefield[22] prepared a chemical fraction called "C substance." Using this material as antigen, she divided the hemolytic streptococci into several groups, designated as A to G, a series subsequently enlarged by the studies of Hare[23] to include Groups H and K. From these investigations came the very useful information that the great bulk of hemolytic streptococci producing disease in man fall into Group A; that strains from Groups F, G and sometimes C are occasionally involved; but that, for practical purposes, the separation of hemolytic streptococci on the basis of whether they are pathogenic or non-pathogenic for man depends

on their identity with Group A. Since almost all strains from all forms of human streptococcal infection belong to Group A, the method gives no direct aid as a possible means of separation of scarlet fever strains from those in other conditions. A method for subdivision within Group A was essential.

Many years before Lancefield's recognition of groups, Dochez, Avery and Lancefield[24] had been able by mouse-protection tests to recognize several serological types among streptococci concerned with human disease. Evidently these represented types within Group A. Bliss,[25] Eagles,[18] Gordon[26] and others studied the possibility of distinguishing types by serological methods, principally that of agglutination. In 1928 Lancefield[27] made another valuable contribution in demonstrating a type-specific "M substance" within members of Group A. By precipitin technic she separated a number of immunologically distinct types. About the same time, Griffith[28] developed an improved method for type differentiation of Group A streptococci by agglutination with absorbed serums. In all, he has distinguished twenty-six types, with a few additional ones as yet unconfirmed. Still other types probably exist, but the extent of type differentiation within the group has probably been quite well defined, because the material studied has been drawn from many different clinical conditions and is of broad geographical distribution.

These improved methods led to work on the problem of whether a single kind of hemolytic streptococcus was regularly concerned in scarlet fever, whether a limited group was involved, or whether any one of the known serological types could at times have a part in causation of the disease. Andrewes and Christie[29] long ago came to the conclusion that no single serological type was involved. Griffith and Gunn[30] found that most scarlet fever strains from England belonged to Griffith's Types 1 to 4, and that while there was relatively wide distribution through his other types, the numbers concerned were small. Equally important was the observation that similar type strains could be isolated from non-scarlatinal infections. Other English workers confirmed these studies. As the methods were taken up in other countries, — in Australia (Keogh et al.[31]), China, most of Europe and some parts of America (Bailey,[32] Pauli and Coburn[33]), — it gradually developed that while most cases of scarlet fever in a given area were related to a limited number of types, nevertheless the types comprising the group varied appreciably from region to region. Practically all the twenty-six recognized types have been found somewhere in the throats of persons with scarlet fever. Furthermore, the many types found in scarlet fever were isolated from time to time from cases of acute tonsillitis, septic sore throat, puerperal fever, erysipelas and a variety of other infectious diseases. Occasionally type strains ordinarily concerned with the production of disease could be found in the throats of apparently normal people. The belief becomes more and more generally accepted that no special kind of streptococcus, distinguished either by its ability to produce erythrogenic toxin or by serological differences, is characteristic of scarlet fever; and that no limited number of serological types is involved, although in a given locality certain ones almost invariably predominate.

From what has been said, it is evident that the mere demonstration of hemolytic streptococci in the throats of persons suspected of having scarlet fever is of itself without value in diagnosis. Clinical and epidemiological evidence must decide this, except that the presence of hemolytic streptococci in appreciable numbers is compatible with the diagnosis of scarlet fever, and that their absence strongly discounts that possibility.

EPIDEMIOLOGY OF STREPTOCOCCAL INFECTIONS

The existing epidemiological problems in scarlet fever seem, then, to resolve into the epidemiology of beta hemolytic streptococcus infection in general. The clinical manifestations of the disease merge into related conditions. This can be demonstrated by field and laboratory studies for individual cases and for groups of cases.

Many epidemics characterized by a predominance of infections with rash have begun with cases of simple angina and upper respiratory infection. Characteristically, classic disease with typical eruption dominates the peak period, with the outbreak frequently tapering off into a variety of atypical and dissimilar infections. The expectancy in sharply defined outbreaks of scarlet fever is a single serological type of hemolytic streptococcus as the infectious agent. Endemic conditions are characterized by a wide variety of types, with some three or four usually predominating. This applies particularly to the scarlet fever that is more or less continuously present in large cities. The clinical nature of the disease as it occurs in a given outbreak is greatly influenced by the relative toxicogenicity and the invasive qualities of the particular strain. Most cases in outbreaks due to types with marked ability to produce toxin, such as Type 10, have classic scarlet fever, with relatively few atypical infections and cases of scarlatinal angina. Epidemics caused by a weak toxin-producer, such as Type 18 may be, are known to include few cases of skin erup-

tion and roughly twenty times that number of sore throats. In epidemics with scarlet fever and scarlatinal angina both fairly frequent, the distribution is characterized principally by sore throats among adults and by scarlet fever among children. Explosive milk-borne outbreaks, originating from a single exposure, often include scarlet fever, tonsillitis and erysipelas as clinical manifestations of infection, indicating that outbreaks tend to breed true according to the streptococcus involved, but not according to clinical disease. Outbreaks of acute respiratory disease of a virus nature—such as measles or influenza—at a time scarlet fever is current can exert a profound influence in extending and quickening its spread. Epidemiological history further reveals repeated episodes in which an outbreak of scarlet fever has been preceded by one of colds or influenza, the two acting independently, but suggesting that the genesis of the scarlet fever outbreak may have been largely conditioned by the preceding epidemic of virus disease.

The principle seems well defined that a program of investigation and control of scarlet fever must deal with the whole group of hemolytic streptococcus infections: it is a streptococcal problem and not one of rashes. Many will ask how necessary is increased emphasis on the control of scarlet fever, with the disease as mild as it is. That depends on what the future holds in respect to scarlet fever, and the answer to that question is wholly speculative. In most parts of the world today scarlet fever is a mild disease, with deaths less than 5 per cent of what they were eighty years ago. The reports of Pope,[34] and of Wilson, Bennett, Allen and Worcester,[35] making use of the long-continued observations in Providence, Rhode Island, show that in 1865 the mortality from scarlet fever in that city was 261 per 100,000. In 1937 the mortality was 2.9 per 100,000.[36] In 1886 about one of every five persons who contracted scarlet fever died. The present ratio is about 1:120. How long this favorable situation will last, no one knows. Extreme variations in severity have occurred, and there is no reason to believe that they will not recur. During the middle of the seventeenth century Sydenham described scarlet fever as extremely mild. It changed character toward the end of the eighteenth century to become a very severe disease. In London from 1804 to 1816 it was again mild, but after 1830 it again became a leading cause of death in childhood, continuing so until the middle of the nineteenth century, when the present progressive downward trend came into play. Knowledge of what to expect in the future may well be aided by more information in respect to some of the epidemiological problems, which are becoming increasingly better defined and appreciated.

25 Shattuck Street.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 25521

PRESENTATION OF CASE

A seventy-eight-year-old widow was seen by her physician because she was extremely nervous and mentally disturbed following an attack of vomiting. On examination she had a temperature of 101.5°F., a pulse rate of 92, a red throat and an occasional fine rale in both chests. On examination her heart was within normal limits; a systolic murmur was heard over the whole precordium. There was an occasional extrasystole. The left patellar reflex was slightly greater than the right. The other tendon reflexes were normal. A blood smear showed an elevated polymorphonuclear count but was otherwise negative. A diagnosis of a mild respiratory infection was made.

The patient was seen again two months later because of increasing nervousness. Her physical examination at that time was essentially negative. The blood pressure was 145 systolic, 95 diastolic. A year and a half later she was examined because of easy fatigability, occasional shortness of breath and slight orthopnea; she used two pillows at night. The heart was then found to be 9 cm. to the left and 3 cm. to the right of the median line. There was marked accentuation of the aortic second sound, and moderate accentuation of the pulmonic second sound. A short systolic murmur was heard over the whole precordium. The pulse rate was 96, and the blood pressure 140 systolic, 80 diastolic. The lung bases were clear; the liver edge was not palpable; there was no edema of the ankles.

Fifteen months later she was seen following an attack of "grippe" that was accompanied by persistent pain in the lower ribs which lasted about six days. Physical examination revealed increased anteroposterior diameter of the chest with hyperresonance, except at the left base below the midscapular region where there was slight dullness, and vesicular breath sounds throughout with no rales but slight decrease in intensity below the angle of the left scapula. The border of dullness of the heart was 8 cm. to the left of the mid-line in the fifth interspace and 3.5 cm. to the right in the fourth. The sounds were distant but clear. There were no murmurs. The blood pressure was 130 systolic, 80 diastolic, in both arms and 150 systolic, 90 diastolic, in both legs. There was no tracheal tug. The pupils were equal and reacted to light and accommodation. The peripheral vessels showed a rather marked degree of peripheral arteriosclerosis. Portable chest plates showed a large round mass, apparently continuous with the heart shadow, occupying the entire middle third of the left lung field. An electrocardiogram showed a sinus tachycardia of 135 beats a minute, with left-axis deviation (−22°), a PR interval of 0.13 sec. and notched P_3 and P_4; QRS_1 and QRS_2 were of fairly low voltage (6 mm. and 5 mm. respectively); ST_1 and ST_2 sagged slightly; T_1 and T_2 were upright; T_3 was shallow and inverted; R_4 was present; and T_4 was upright. A blood Wassermann test was negative.

Following this short illness she went to Florida for several weeks and felt well. A few months later, she became weak and tired and had slight low-back pains with a little gas. On the day before her death she spent a busy day shopping, apparently feeling quite well. She went to bed at 9:00 p.m. after a good supper, slept quietly until midnight when she suddenly awoke and complained of severe pain in the mid-upper back and chest. She became extremely orthopneic and dyspneic. On the arrival of her physician a few minutes later she was sitting up in bed, breathing rapidly (40 to 50 respirations per minute). Her pulse was 140 and weak. She was wild-eyed, and there was an ashen cyanosis, with cold sweat. The peripheral veins were not distended. The heart sounds were distant but clear. There were no murmurs. The lungs were clear throughout; there were no rales even at the extreme bases. The abdomen was negative. The patient was given 1/4 gr. of morphine sulfate and 1/150 gr. of atropine sulfate. Although rapid respirations persisted she soon became unconscious. At about 1 a.m. the radial pulse became imperceptible and the blood pressure could not be measured. Oxygen therapy was given for an hour. An electrocardiogram showed a ventricular and auricular rate of about 130 with slight left-axis deviation, an upright T_1 and T_2 and an inverted T_3; there was a PR interval of 0.15 sec., and a slightly elevated ST_1, ST_2 and ST_3, with low voltage. The patient was given Coramin and caffein and sodium benzoate but expired about two and a half hours after the onset of the attack.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS: There is nothing in the record of the first episode to influence one to alter the diagnosis made by the patient's physician of mild respiratory infection. Nervousness, vomiting and a slight inequality of the patellar reflexes occurring in a patient of seventy-eight apparently put the physician on his guard for a

mild cerebral vascular accident. But he obviously found no conclusive signs. Without at least a Babinski sign on one side, demonstrable weakness of a muscle group or some other neurologic sign, an attack of mental confusion or other indication of cerebral insult, slight thrombosis or hemorrhage would have to be dismissed, and the inequality of the patellar reflexes disregarded. Nervousness, in my experience, is to be expected in any old person who is ill. Such patients are always apprehensive. The systolic murmur over the precordium is also relatively unimportant. Basal systolic murmurs due to dilatation of the aorta and apical systolic murmurs due to relative mitral insufficiency are common in the aged.

Examination two months later contributed nothing of importance. Nervousness was still present, and hence not due, as we supposed earlier, to the acute illness alone. The history does not indicate whether there were any disturbing influences in the home environment or elsewhere to account for this symptom.

At the time of the third examination she had easy fatigability, occasional dyspnea and orthopnea. The last two, one could assume, were signs of beginning myocardial insufficiency. The heart was not large to percussion, but the measurements were perhaps not too accurate, for we note further along in the record that the lungs were hyperresonant. If they were hyperresonant fifteen months later they were probably hyperresonant at the time of this examination, although no mention is made of the fact. Further evidence of beginning left ventricular failure is provided by the accentuation of the pulmonic second sound and the lowering of the diastolic pressure from 95 — which was reported eighteen months earlier — to 80.

Fifteen months later, at the age of eighty-one, the patient developed a pain in the lower ribs which lasted for six days following an attack of "grippe." One is always suspicious of a diagnosis of "grippe," and since here it is in quotation marks, one wonders whether it was made by the patient and not by her physician. Such lay terms as "grippe," "cold" and "gas" often confuse the issue for the doctor unless he is able by careful questioning to get a much clearer idea of just what the patient is attempting to describe. If she actually had a respiratory infection one might be justified in attributing the pain in the lower ribs to acute pleuritis occurring with or without a mild attack of pneumonia. Such a supposition would be more tenable if a relation between pain and respiratory movements had been established. Herpes zoster hardly requires consideration; the typical eruption should certainly be present six days after the onset. There is no mention of restriction of motion or pain on movements of the trunk which might suggest muscular strain or arthritis of the spine as a cause of this discomfort. When pain of this type occurs, and the more usual causes are not demonstrable, one must always think of the possibility of pressure or root pain. I am willing to wager that it was because of this possibility that the patient's physician had her x-rayed so promptly. Or perhaps he was confused, as he justifiably might have been, by the pulmonary signs — slight dullness and diminution of breath sounds in the left scapular region. These are not the signs of pneumonic consolidation or pressure atelectasis. Bronchial breathing or at least bronchovesicular breathing would be expected with either of these disorders. A localized area of fluid, too, would be more likely to cause diminished bronchial or bronchovesicular breathing than it would diminished vesicular breathing. The most tenable explanation of these signs, it seems to me, is that pressure on a bronchus prevented aeration of a small area of the lung. Yet, not enough lung tissue was affected to cause total absence of sounds because of the presence of unaffected lung surrounding the involved area. X-ray films demonstrated a large mass which must have been tumor, aneurysm or perhaps an encapsulated collection of fluid. At this point I shall ask Dr. Holmes to discuss the x-ray film, although I wonder whether without lateral plates and the benefit of fluoroscopy he will be able to differentiate the various possible causes of the shadow.

Dr. George W. Holmes: There is an obvious mass in this region. It is round, not lobulated. It does not displace the heart or mediastinum. It may to some extent press on the bronchus because there is not much air in the lower part of the chest. The diaphragm is a little elevated, high on both sides. The heart shadow, so far as I can make out, is slightly enlarged, with the left ventricle more prominent than normal. It would make me suspect slight hypertrophy of the left side of the heart — very little though. I cannot see any evidence of calcification in the walls of this mass. I do not know that I would put much weight on a film like that. What we should like to have is a fluoroscopic observation, and films taken with the Bucky diaphragm to give us detail and films taken in the oblique and lateral views. I presume this patient was too sick to have that done. Such a mass as that with the evidence I have here could be either a tumor or a very tortuous aorta. I do not believe it is a tortuous aorta because it is a little larger than

we should be likely to see, and it shows some evidence of pressure on the bronchus, which would not be produced by a dilated aorta. I think it is definitely a tumor. It is in the region of the descending loop of the thoracic aorta.

DR. ADAMS: The electrocardiographic report seems to throw very little light on the situation. I am sure Dr. White, since he is here, will give us the benefit of his interpretation of the tracing.

DR. PAUL D. WHITE: There is not a great deal out of the way in this first record. There are minor variations from the normal, perhaps a little more left-axis deviation than usual but close to the borderline. There is nothing indicating an acute process in the heart in the first record, nor in the last record. There is little difference between them. There is a statement that there was low voltage, but the voltage is actually just within normal limits and does not indicate any serious process. In other words these are fairly good records for a woman eighty-one years old.

DR. ADAMS: Following this illness the patient went to Florida. I see no reason why she should have been prevented from so doing. Certainly with a mass of this size, no matter what it was, there was very little in the way of treatment to be offered, especially in a person of her age. Her condition remained essentially unchanged for a few months except for weakness, easy fatigability and low-back pain, until the final episode which occurred suddenly.

In the middle of the night something happened, and within a few hours she was dead. Of what did she die? And what is the relation of the mass to death? Should one hook them together? The usual medical causes of death occurring within an hour or so are cardiac failure, pulmonary embolism, coronary thrombosis and cerebral hemorrhage. The last named may be promptly excluded without comment. If the patient had had sudden left ventricular failure she would certainly have had, during the subsequent two hours of her life, the signs of acute pulmonary edema, rales in the chest and bloody sputum. If she had had right ventricular failure there would have been more cyanosis and distention of the cervical veins. Furthermore, we have no reason to suspect either of these in a person previously well and without any appreciable degree of heart disease. With extensive pulmonary embolism, too, there would have been more cyanosis and distention of the cervical veins, and there is no reason to presuppose a source for an embolus. Coronary disease is somewhat more difficult to exclude but it seems unlikely because of the severity of the pain in the back, which is rare with coronary thrombosis, and because, if it took her two hours to die following an attack of coronary thrombosis, some of the signs of heart failure just discussed would have developed. Added evidence that the coronaries were not involved is provided by the electrocardiogram, although electrocardiographic changes might not occur as early as two hours after the onset of such an episode.

DR. WHITE: She was very sick; I think we should have expected more evidence in the electrocardiogram if acute coronary thrombosis were responsible for such a grave condition.

DR. ADAMS: It is necessary, therefore, to find some other cause of this sudden demise, and naturally one turns to the mass and quite logically wonders whether it was responsible. The mass must have been tumor or aneurysm. I fail to see how a benign tumor could account for the terminal picture. Such a tumor, by pressure on the trachea, might conceivably cause sudden death, but lesser attacks of respiratory distress should have preceded the final attack, and the patient obviously did not die of suffocation. A malignant tumor would probably have given more signs previous to the terminal episode, such as harrassing cough, bloody sputum or, if the apex of the lung were involved, Horner's syndrome. One would also expect more evidence of systemic disease, such as loss of weight, anemia or even greater weakness. Furthermore, a malignant tumor as large as this one would probably show, by roentgenogram, extension of the process into the right side of the chest.

If we exclude tumor — and I think we have done so — then we are forced to the conclusion that this patient had an aneurysm and died of rupture. The clinical picture of the terminal event is consistent with this diagnosis. Sudden pain in the back suggests a perforation. The ashen cyanosis, cold sweat, weakening of the pulse and elevation of its rate are typical of circulatory collapse or hemorrhage. If she had aneurysm, what kind of aneurysm was it? There is no evidence of syphilis: the patient was old for a syphilitic aneurysm, and the Wassermann reaction was negative. The latter does not exclude the disease, although it is strong evidence against it. A negative Hinton test would be even stronger evidence, for this test is rarely negative in the presence of cardiovascular syphilis. Could it have been a dissecting aneurysm? It could have been, but usually with dissecting aneurysm one finds pain gradually extending farther and farther down the back, and often pain in the arms produced by the involvement of the subclavian arteries. Moreover, in my experience, dissecting aneurysm occurs only in patients with hypertension. Now, having already ex-

cluded dissecting aneurysm and having excluded syphilitic aneurysm I am forced into the unhappy position of having to make a diagnosis of saccular aneurysm due to arteriosclerosis. Can arteriosclerosis cause saccular aneurysm? Yes, it can, although very rarely. I have had in my own practice one case of saccular aneurysm due to arteriosclerosis, but this was in the abdominal aorta. It was proved at postmortem examination. I personally have never seen a saccular aneurysm in the chest due to arteriosclerosis, but if it can occur below the diaphragm I fail to see why it cannot occur above. I am by no means unaware of the fact that I am treading on thin ice in making a diagnosis of such a rare disorder, but I believe, nonetheless, that this patient had a saccular aneurysm secondary to arteriosclerosis and that rupture of the aneurysm with resultant hemorrhage was the immediate cause of death. Ruptured aneurysm due to syphilis would be my second choice.

Dr. Tracy B. Mallory: Does anyone desire to disagree with Dr. Adams?

Dr. J. H. Means: I should like to ask Dr. Holmes if the intrathoracic mass could have been a goiter?

Dr. Holmes: I suppose it is a possibility, but a very unlikely one.

Dr. Means: Some large intrathoracic goiters stick down, in a general way, more or less as this mass does. Also may I ask, could it have been an aneurysm of the heart?

Dr. Holmes: No.

Dr. Means: I am interested in what this patient's condition might have been before the terminal episode. We are told that she had weakness and nervousness which Dr. Adams was inclined to dismiss. I am not certain they should be dismissed. When, in an elderly person, they are combined with tachycardia, wide pulse pressure and symptoms suggesting low-grade cardiac insufficiency, they suggest thyrotoxicosis. I should like to know whether she had ever had digitalis or iodine, and, if so, what effect it had on her.

Dr. Henry D. Stebbins: She had never had either.

Dr. Adams: I discounted the weakness and nervousness, Dr. Means, because it seems to me that a patient of this age would almost be expected to have both.

Dr. Chester M. Jones: When was the x-ray film taken in relation to pain in the back?

Dr. Stebbins: It was taken four months and three weeks before the attack of pain.

Dr. Jones: The death suggests hemorrhage.

Dr. Mallory: I should like to hear a surgical opinion.

Dr. Edward D. Churchill: Because of the statement on the day before death that she felt well, spent a busy day shopping and ate a good supper and went to bed, I am inclined to agree with Dr. Adams. It would take something abrupt to kill a person that quickly. I think of hemorrhage from a dissecting aneurysm.

A Physician: I should like to ask Dr. Adams whether the possibility of thoracic tumor with erosion of a vessel followed by hemorrhage should be considered.

Dr. Adams: Yes, that is a possibility. My experience with intrathoracic tumors is limited, but as I pointed out earlier I should expect the patient to have had cough, bloody sputum or by x-ray some evidence of tumor in the right side of the chest as well as the left. A fluoroscopic examination showing the presence or absence of pulsation would have been helpful, although not conclusive, for with tumor, pulsation can be transmitted from the aorta and cause a mistaken diagnosis of aneurysm.

Dr. Mallory: Dr. Stebbins, you had the care of this patient. Have you anything to add?

Dr. Stebbins: No. I know the answer, so probably I had better not add anything, but I should be glad to answer any questions.

Dr. Churchill: What was your diagnosis?

Dr. Stebbins: Mine was the same as that of Dr. Adams and Dr. White, who also saw the patient.

Dr. White: I saw her during the last ten minutes of her life and have nothing to add. It certainly was striking, as Dr. Churchill has said, that she had been well and very active that day and that she suddenly became acutely ill and died so quickly. We suspected that death was due to rupture of an aortic aneurysm and not to heart failure or coronary disease.

Dr. Means: The x-ray film was taken some time before death. If she died of ruptured aneurysm, the story suggests dissecting aneurysm more than it does syphilitic aneurysm. The x-ray picture is certainly not that of dissecting aneurysm.

Dr. Holmes: I should be inclined to agree with that.

Dr. Means: I think she could have had a dissecting aneurysm. However, Dr. Adams was talking along the lines of syphilis, which I think is unlikely.

Dr. Adams: You must have misunderstood me, Dr. Means. My first diagnosis was arteriosclerotic saccular aneurysm. Syphilis is a possibility, but unlikely.

Dr. Churchill: It is rare to get a dissecting aneurysm in the presence of hypertension.

DR. ARTHUR W. ALLEN: I think she lived too long for a patient with a ruptured saccular aneurysm — two and a half hours.

DR. ADAMS: The patient whom I mentioned with abdominal aneurysm lived for forty-eight hours after the rupture.

CLINICAL DIAGNOSIS

Ruptured dissecting aneurysm of aorta.

DR. ADAMS'S DIAGNOSIS

Arteriosclerotic saccular aneurysm, with rupture.

ANATOMICAL DIAGNOSES

Arteriosclerotic aneurysms of aorta, multiple, with rupture of one into right pleural cavity.

Aneurysm of the left common iliac artery, arteriosclerotic.

Hemothorax, right.

Pulmonary atelectasis, compression of left lower lobe.

Arteriosclerosis, marked, aortic; slight, coronary and renal.

Operative scars: simple mastectomy, right; appendectomy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At postmortem the right pleural cavity contained 2000 cc. of blood. On tracking down the source of the hemorrhage a large, saccular intrathoracic aneurysm of the descending aorta was found. There was another smaller thoracic aneurysm and a large abdominal one, and there was a fourth aneurysm of one of the iliac arteries. I think that the multiplicity of aneurysms in this case might have been determined on physical examination. Perhaps both the one in the iliac artery and the one in the abdominal aorta could have been felt if examination had been made specifically for that possibility. She was obese, however, and it might not have been possible. The aneurysms showed very calcareous walls, with no evidence of syphilitic aortitis, and are definitely of the arteriosclerotic type. It is rather characteristic of such sclerotic aneurysms to appear in the abdominal rather than the thoracic aorta, but they can occur in either place. There was no histological evidence of syphilis, and I think we can accept the serological test as having been verified.

DR. WHITE: It is the first case of the sort I have ever seen, and I wonder what your experience has been here with arteriosclerotic aneurysm.

DR. MALLORY: We have seen very few in the thoracic aorta, but they are not infrequent in the abdominal portion. Two other favorite locations are the iliac and the popliteal arteries.

DR. WHITE: How were the coronaries?

DR. MALLORY: There was no marked degree of atheroma and no narrowing anywhere.

DR. WHITE: It seems to me that an arteriosclerotic aneurysm is a condition not well recognized in the literature, at least so far as the thoracic aorta is concerned. Our cases ought to be collected and reported.

CASE 25522

PRESENTATION OF CASE

A twenty-eight-year-old Polish grocery clerk entered the hospital because of pain and swelling of the right elbow.

Twelve months before admission the patient wrenched his right elbow while cranking an automobile. The soreness which resulted disappeared without treatment, and except for slight aching, he was well until about six weeks before entry when the joint "snapped" during an act of normal movement. It became hot, red, swollen and tender. He noted a scraping feeling on moving the joint, and there was limitation of both flexion and extension. His physician took x-ray films of the part and aspirated fluid from the joint but was unable to make a definite diagnosis. Following aspiration the pain diminished for a while, but soon returned. He noticed no other symptoms.

Physical examination revealed a very apprehensive, hyperactive, co-operative young man in apparent acute distress. The left elbow was slightly swollen but not hot; there was fullness over the head of the radius. The right elbow measured 26 cm. in circumference, the left 23.8 cm. Motions were limited on the right as follows: supination, 20°; extension, 40°; flexion, 110°; pronation, normal. Motions on the left were normal. On pronation and supination there was an occasional grating in the elbow, with tenderness over the radial head, olecranon and medial epicondyle. The heart, lungs and remainder of the examination were negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,450,000 with 15.3 gm. hemoglobin (photoelectric cell method), and a white-cell count of 11,500 with 63 per cent polymorphonuclears. The urine examination and blood Hinton tests were negative. The spinal-fluid protein was 52 mg. per 100 cc.; the gold-sol and Wassermann tests were negative.

On the sixth hospital day an operation was performed.

Differential Diagnosis

Dr. Edwin F. Cave: In discussing this case, it seems important to decide whether the disease originated in the joint itself, in the bursa or bursas about the joint or in the ends of the bones that go to make up the joint. It impresses me as being a case of disease of the joint itself, a case of mild trauma with superimposed infection of some nature. Several possibilities come to one's mind. Here is a young man of twenty-eight, apparently a husky fellow who did relatively heavy work and subjected all his joints to strenuous activity. It is, therefore, not unlikely that there has been sufficient trauma to the elbow joint, either by excessive strain or by direct blow, to result in aseptic necrosis of the joint cartilage, and finally the development of an osteochondritis. We do know that such a condition occurs in the elbow second in frequency only to that of the knee joint. But, this alone will not explain the findings in the particular joint under discussion. If we are dealing with osteochondritis there must also be superimposed infection of some nature. The essentially normal blood, — except for slight elevation of the white-cell count, — the normal temperature and pulse are against any virulent infection. The duration of six weeks is also against that. The fact that he had mild symptoms for a period of ten and a half months before the acute process developed suggests that there was latent infection present during this time. I do not believe that this is a case of infectious arthritis, and tumors of bone in this region are rare. Ewing's tumor does not occur in such close proximity to joints, and a normal temperature is also against this diagnosis. Osteomyelitis of the humerus, ulna or radius in this region is a remote possibility, and could account for the joint swelling, but again this condition is rare in this region, and probably could be ruled out by the blood findings, normal temperature and pulse. Syphilis may be discarded because of the negative blood Hinton, spinal-fluid Wassermann, and gold-sol curve.

The two possibilities which impress me as being most likely are: Neisserian infection of the elbow joint and tuberculosis. The duration of symptoms and the apparent acuteness of the joint are not inconsistent with the diagnosis of gonococcal infection. If this is the diagnosis, I am certain that the infection had been present only for six weeks, and had nothing to do with the mild symptoms in the joint during the past year. I do not believe, however, it could be due to the gonococcus because of the relatively low white-cell and polymorphonuclear counts and the normal temperature.

I think it could perfectly well be due to tuberculosis, and that is my diagnosis. His age and the duration of symptoms are consistent with this diagnosis. We should like to know what x-ray films of the joint showed, what the tuberculin test was, and whether any lesion was demonstrable in the chest plate. The slight elevation in white count and the polymorphonuclear count of only 63 per cent, hence a relative lymphocytosis, furnish confirmatory evidence for the diagnosis of tuberculosis.

The swelling of the opposite elbow is difficult to explain, but this may also be due to tuberculosis, because we know that in a series of 215 cases of spinal tuberculosis in this hospital, between one fourth and one third had more than one joint involved. This statement also holds true in a group of 90 children at the New England Peabody Home for Crippled Children. It may be that in the left elbow we are dealing with a synovial type of tuberculosis without demonstrable lesion by x-ray.

Clinical Diagnosis

Traumatic arthritis, ? loose bodies.

Dr. Cave's Diagnosis

Tuberculous arthritis of the right elbow.

Anatomical Diagnosis

Tuberculous arthritis of the right elbow.

Pathological Discussion

Dr. Tracy B. Mallory: The joint was explored, and the surgeon found that the joint space was filled with so-called "rice bodies" and, on further exploration, that there was a sizable cavity in the olecranon and another in the coronoid process. The joint cartilage was eroded in several spots, and the entire picture was quite typical of tuberculosis of the joint; the diagnosis was confirmed by microscopical examination. A fusion was performed, and the patient had a fairly quick and satisfactory convalescence.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
The New Hampshire Medical Society
The Vermont State Medical Society

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

—AND A HAPPY NEW YEAR

We have come to think of our New Year greeting, perhaps, too much in reference to the day, and not enough in reference to the year, as was undoubtedly its original intention. Christmas is our day of festival, a day with double meaning, derived from a spiritual satisfaction at the birth of our accepted religious leader and from an older, more sensuous satisfaction at the beginning of the return of the sun to northern latitudes and the consequent lengthening of the days.

It is appropriate that, as the shortest day is passed and the hours of sunlight begin to increase, we should reckon our new year as beginning. With and between the two holidays we have our one Christian festival season marking the beginning of a new era in man's relations to man and the start of a new year in which to put these relations into effect. After the Christmas–New Year holidays we have our winter, but after them we have also the sun's northward journey to watch and to mark off on our calendars, until the coming in of spring.

Our "Happy New Year," then, connotes more than a day on which to express a greeting and to congratulate ourselves and each other on living in a hemisphere at peace and in relative prosperity. It is the introduction to another year—a new cycle of seasons through which we strive to live as successfully, as efficiently and as happily as our inner resources permit.

One of the happy functions of New Year's Day is to afford an opportunity of brushing up on our good resolutions for the incoming year. This is sometimes a source of cynicism or mirth because resolutions so seldom last throughout the twelve months. This does not detract from their value. A good suit also needs to be brushed and pressed, and shoes to be polished. The more use they are to us, the more they need these services. The refreshening of resolutions does not mean that they are for show only, but that they have merit. The new year offers a particularly appropriate opportunity for setting our individual houses in order.

A NEW LIBRARY OF MEDICAL HISTORY FOR YALE

A library devoted to the history of medicine has recently been established at Yale University School of Medicine. A building is about to be erected, which will contain, in addition to the material already available, three important collections of books. The first is that of the late Dr. Harvey Cushing. This collection, one of the most important private medical libraries in the world, is particularly rich in material relating to Vesalius

and the pre-Vesalius anatomists. In addition, there are many books on surgery, including a superb collection of volumes by Paré and hundreds of items on medical education, schools, biographies, histories and material of a similar character. Secondly, there is to be added to this the library of Dr. John F. Fulton, Sterling Professor of Physiology, Yale University. His collection of books is also notable, for it contains the fundamental physiological treatises of the past, as well as a large number of purely literary contributions by physicians and scientists. Fortunately there is little duplication in the two collections. Finally, word has been received from Switzerland that the library of Dr. Arnold C. Klebs, an old friend of Dr. Cushing, who has lived in Switzerland for many years, but who is an American citizen, will be added to the two collections mentioned above. Dr. Klebs's collection, again, is unique and different from that made either by Dr. Cushing or by Dr. Fulton. His primary interest has been in the printing of early books, especially those issued in the fifteenth century that were of a medical or scientific nature. His library consists largely of the apparatus useful to a medical or scientific bibliographer. It is not rich in early printed books themselves, but is a most unusual collection of books about books, printers, type, paper and other aspects of the printing trade before 1500.

To house these collections a new wing is being added to the Sterling Hall of Medicine, with room for about 400,000 volumes. In one part of the building will be the historical collections noted above and in another a working library for the medical school. The building, on the medical school grounds and adjacent to the New Haven Hospital, will form an integral part of the Yale medical unit.

Dr. Cushing's collection of books is so important that its acceptance by Yale University is an epoch-making step. New Haven will become a center for students of medical history such as has not been developed elsewhere, except possibly in the home of the greatest collection of all, the Army Medical Library in Washington. The new library will form, moreover, a link in a chain of medical libraries extending from Montreal through Boston, New Haven, New York, Philadelphia and Baltimore to Washington. By traveling this path a scholar of medical history will have available to him the most significant books dealing with medicine in the past. The Yale link in the chain will be by no means a weak one, for the collections given by Cushing, Fulton and Klebs form a nexus of great strength. Yale University is to be congratulated on visualizing the importance of these collections and seeing that they are suitably housed.

OBITUARY

SUMNER MEAD ROBERTS

1898 – 1939

Sumner M. Roberts was instantly killed in an automobile accident November 19, 1939.

He was born on January 25, 1898, in Dedham and attended the public schools there as a child. His family moved to Chestnut Hill when he was about ten, and he then entered the Country Day School, where he prepared for college. At the latter he was a member of the football, track and baseball teams and of the student council. Then he went West for a year to the Mesa School at Phoenix, Arizona. During his first year at Harvard College, which he entered at the age of eighteen, he was on the freshman football and baseball squads. When the War came on and called him, he elected to enter the naval service. For preliminary training he shipped as a member of the crew of a South American cargo boat, then entered the Naval Reserve and went to school at Charlestown. He was commissioned as ensign in the United States Navy but never went to sea. He was discharged soon after the Armistice and re-entered Harvard College. During the following summer he went to Hawaii with Charles Thorndike to work with Dr. Thomas A. Jagger, who was engaged in the study of the crater of the volcano, Kilauea.

He was graduated from Harvard College in 1921, with a war degree of A.B., having taken special courses in zoology and biology. After four years at the Harvard Medical School, he received an appointment as surgical intern at the New

York Hospital, working under Dr. Eugene H. Pool. He then took a two-year postgraduate course in orthopedic surgery under the auspices of the Harvard Medical School, the Children's Hospital and the Massachusetts General Hospital. On completing his medical training he entered private practice and became associated with Drs. Robert B. Osgood, Philip D. Wilson and Francis C. Hall at 372 Marlborough Street.

He was assistant visiting orthopedic surgeon at the Massachusetts General Hospital, consulting surgeon at the Robert Breck Brigham Hospital and assistant in orthopedic surgery at the Harvard Medical School. He was a member of the American Medical Association, Massachusetts Medical Society, American College of Surgeons, Aesculapian Club, American Academy of Orthopaedic Surgeons and American Orthopaedic Association. He was president of the Boston Orthopaedic Club at the time of his death.

He was married on December 27, 1927, to Elizabeth Converse, the daughter of the eminent musician and composer, Frederick S. Converse. He is survived by his widow and three children.

The swift communication of the news of his untimely death by word of mouth from friend to friend and the immediate sense of grief which fell on all testify only too well to the affection and respect which his personality had engendered. He was straightforward and sincere. Courage and simplicity, which love of the outdoors seems to breed, were his in abundant measure. He found a pleasure in the lonely wood and at the shore which gave him peace of mind and tranquillity, undisturbed by trivial things.

Professionally he received an excellent training and then chose orthopedic surgery as his field. The treatment of fractures and the rehabilitation of the severely crippled arthritic patient were problems which particularly interested him, and his contributions to the knowledge of these subjects are of lasting merit. His patients, including those on the hospital wards, regarded him with trust, and each was rewarded by a well-planned and dexterously executed attempt at cure or amelioration of his afflictions.

His modesty and reserve prevented him from becoming a favorite of the crowds, but few physicians can number more sincere friends than he among their colleagues. At the zenith of his ability, but before the great honors which were rightly his had sought him out, his life was taken. We have lost a great physician, even as his family has lost an exemplary husband and father.

J. S. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

FATAL PUERPERAL SEPSIS FOLLOWING FORCEPS DELIVERY

Mrs. B. A., a twenty-eight-year-old woman, was admitted to the hospital on March 24, 1926, complaining of acute severe abdominal distention with copious black vomitus. A para I, she had been delivered at home with forceps on March 21. Vomiting, dehydration and abdominal distention had followed the delivery. The patient had also had continuous abdominal pain, which had begun on March 23. The family history and past history were not obtained.

On entry the temperature was 101.6°F., the pulse 136, and the respirations 40. The patient was toxic, dehydrated and febrile, with a markedly distended, extremely tender, spastic abdomen, especially in the hypogastrium. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. A rectal examination was negative. The white-blood-cell count was 3800, and the urine showed pus and casts.

She was given immediate gastric lavage, subpectoral fluids, enemas, rectal fluids, posterior pituitary extract, and flaxseed poultices to the abdomen. The patient's course was progressively downhill, and she became more and more toxic, irrational and distended. Just before she expired on March 25 the temperature was 105.2°F., the pulse 160, and the respirations 36.

Comment. The case of this patient, who had vomiting, abdominal distention and fever thirty-six hours after delivery, suggests that the uterus had been partially ruptured in the lower segment. The abdominal symptoms of peritonitis occurred much more quickly than they would have if the infection were limited to the uterus. No blood culture or uterine culture was taken. The patient was apparently a very sick woman at the time of entry, and her best chance of recovery lay in following strict conservatism.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

DEATHS

MEAD — George N. Mead, M.D., of Winchester, died December 14. He was in his eighty-first year.

Born in Concord, New Hampshire, he graduated from Phillips Exeter Academy and attended Harvard University. He received his degree from Harvard Medical School in 1886, and interned at the Massachusetts General Hospital. He practiced for a short time in Everett and then joined the staff of the Winchester Hospital. Dr. Mead retired from active practice in 1929.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and a son survive him.

SCHMIDT — Richard D. Schmidt, M.D., of Dorchester, died December 18. He was in his sixty-ninth year.

Born in Roxbury he attended public schools in Boston and Brooklyn, New York, and became a registered pharmacist before entering medical school. He received his degree from Tufts College Medical School in 1904.

Dr. Schmidt was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a brother, Dr. Frederick Schmidt, survive him.

MISCELLANY

ANNOUNCEMENT OF THE FRANCIS AMORY SEPTENNIAL PRIZE OF THE AMERICAN ACADEMY OF ARTS AND SCIENCES UNDER THE WILL OF FRANCIS AMORY

In compliance with the provisions of the will of the late Francis Amory, The American Academy of Arts and Sciences, as trustees of a fund given by the testator, announces a prize to be known as the Francis Amory Septennial Prize to be awarded for conspicuously meritorious work performed during the immediately preceding septennial period "through experiment, study or otherwise, in the treatment and cure of disease and derangement of the human sexual generative organs in general, and more especially for the cure, prevention or relief of the retention of urine, cystitis, prostatis, and so forth." While the donor wished especially to reward the discovery of any new method of treatment, he expressly authorized that the prize might be given to any author who might have contributed any theoretical or practical treatise of extraordinary or exceptional value and merit on the anatomy of said organs or the treatment of their diseases.

If there shall appear work of a quality to warrant it, the first award will be made in 1940. The total amount will exceed $10,000, which may be divided at the discretion of the Academy among several nominees. While formal nominations are not expected and no essays or treatises in direct competition for the prize are desired, the Committee on the Francis Amory Septennial Prize invites suggestions looking toward the wise performance of its duty. Communications on this subject should reach the committee not later than May 15, 1940, and should be addressed in care of the American Academy of Arts and Sciences, 28 Newbury Street, Boston. The members of the committee are: Dr. Roger I. Lee, chairman, Dr. Walter B. Cannon, Dr. David Cheever, Prof. Leigh Hoadley, Dr. William C. Quinby, Dr. Ernest E. Tyzzer and Dr. Soma Weiss, secretary.

NOTE

The Committee on Faculty of Middlesex University has announced the appointment of Dr. Karl Singer as associate professor of physiology in the School of Medicine. Dr. Singer was born in Vienna, where he received his medical degree in 1927. He served as acting superintendent of the Kaiser Franz Joseph Hospital and as a member of the Department of Hematology of the University Clinic in Vienna. For ten years he was an associate in applied physiology in the University of Vienna Medical School and research fellow of the Academy of Sciences. He came to Boston last year, where he became a research fellow in hematology at the Beth Israel Hospital.

CORRESPONDENCE

A FAIRY TALE

To the Editor:

Once upon a time a citizen who had a controlling interest in a successful drug emporium and was philanthropically inclined decided that people needed an extension or alteration of medical services. So, he formed a charitable corporation with his niece and the druggist's son as the salaried agents of the corporation. Then he made an agreement with a doctor who had an office nearby that the niece should collect all fees paid to the doctor, retain 20 per cent for operation of the charitable corporation and return 80 per cent to the doctor. The druggist, who received no salary from the corporation, suggested that people go to see the doctor because he was well equipped with all kinds of stethoscopes, cystoscopes, proctoscopes, electrocardiographs and x-ray apparatus and had young men do work which he himself did not wish to do or did not feel qualified to do. The charitable corporation soon suggested that tickets for medical care be issued and sold in blocks at reduced prices, and a little later that tickets be sold annually to cover all medical services. The druggist continued to urge people to go to the doctor whose office was near the store. By the same token the drug emporium was near the doctor's office. The druggist, the citizen and their families spoke to friends about the wonderful new plan and urged that they all leave their present doctors and join up. The citizen was even invited to speak before groups in churches, to mercantile associations and in stores where there were considerable numbers of employees. (Of course, the doctor who was under contract with the charitable corporation, *never* himself solicited anybody to come to him.)

This is the first installment of the fairy tale. Perhaps some other member or members of the Massachusetts Medical Society would write the second installment, telling what happened to the quality of medical practice given the people of the community during the succeeding ten or twenty years.

David Halbersleben, M.D.

3 Conway Street,
Roslindale, Massachusetts.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor: In addition to the articles enumerated in our letter of November 2 the following have been accepted:

International Vitamin Corporation

I. V. C. Ascorbic Acid Tablets

I. V. C. Thiamin Chloride Crystalline Tablets, 0.5 mg.

I. V. C. Thiamin Chloride Crystalline Tablets, 1.0 mg.
I. V. C. Thiamin Chloride Crystalline Tablets, 3.3 mg.

Mead Johnson & Co.
Mead's Mineral Oil with Malt Syrup

New York Quinine and Chemical Works
Nicotinic Acid—N. Y. Q.

Parke, Davis & Co.
Vitamin K in Oil
Capsules Vitamin K in Oil

PAUL NICHOLAS LEECH, *Secretary*.

535 North Dearborn Street,
Chicago, Illinois.

REPORTS OF MEETINGS

PALMER MEMORIAL HOSPITAL

A symposium on cancer of the tongue was held on Tuesday, June 13, at the Palmer Memorial Hospital, with Dr. Leland S. McKittrick presiding. The discussion was conducted by the staffs of the Massachusetts General, Huntington Memorial, Pondville and Palmer Memorial hospitals.

The first speaker, Dr. Ira T. Nathanson, of the Huntington Memorial Hospital, reported on 387 primary cases of cancer of the tongue treated at that institution between 1922 and 1936. Of these only about 35 per cent were in Group 1A, that is, without palpable nodes of any sort on admission. Cure of the local lesion was accomplished in 39 per cent of the Group 1A cases and in 16 per cent of the Group 1B cases. Dr. Nathanson found duration of the lesion to be insignificant but size and position on the tongue of great prognostic import in local cures for both groups.

In the development of metastatic nodes in the neck, the grade and size of the primary lesion played an important role, and these same factors were not significant in affecting the curability of the nodes. As in the primary lesion, duration of the disease was not a factor. Size of the nodes could not be taken as a positive criterion of malignancy, for 76 per cent of those which were 1 cm. or less in diameter were eventually malignant. When nodes were more than 1 cm. in diameter, over 95 per cent were malignant.

Of those subjected to radical surgery, there was a 25 per cent cure of those with positive cervical nodes. Cures of three years or more were obtained in 31 per cent of the Group 1A cases and in 8 per cent of those in Group 1B, with a total salvage for all cases of 15 per cent.

Dr. Nathanson concluded that operable and accessible lesions seemed to be offered the best chance of local cure by surgery, but admitted that insufficient treatment had been given in comparable irradiated cases. If no nodes were palpable in the neck, or were palpable but less than 1 cm. in diameter, and if the primary lesion was small and of low-grade malignancy, one was justified in careful surveillance of the nodes since their curability was not influenced by their palpability. However, when the nodes were 1 cm. or greater in diameter, especially if the primary lesion was higher than Grade I and larger than 1 cm., rigorous treatment was to be directed toward the nodes. Management of the lymph nodes, however, should not be undertaken until the primary lesion has been cured or brought under control.

Dr. Roy E. Mabrey presented 106 cases of cancer of the tongue treated from 1927 to 1935 at the Massachusetts General Hospital. Pathological study of cervical nodes removed surgically indicated that large primary lesions were prone to give rise to positive nodes, and that large nodes were likely to be positive. Some palpable nodes, however, were negative at operation, whereas some non-palpable nodes showed evidence of metastasis.

Cure of the local lesion resulted more often in cases with anterior lesions, and surgery gave the best therapeutic results, as at the Huntington Memorial Hospital. Three-year cures in Group 1A amounted to 20 per cent, and in Group 1B to 0.6 per cent, with a total salvage of 11 per cent for the entire group. Cures were obtained in 39 per cent of those treated surgically; the operative mortality was 11 per cent.

Dr. Clifford C. Franseen reported the results of 50 cases from the Palmer Memorial Hospital. In regard to possible etiologic factors, leukoplakia was mentioned as a definite precursor in 20 per cent, syphilis in 18 per cent, and poor teeth in 24 per cent of the cases; but Dr. Franseen ventured that a greater number would be found to have leukoplakia if the condition were sought and its presence recorded.

Of those treated by surgery alone 29 per cent were cured for three years or more, and there was a 15 per cent operative mortality. The gross salvage on all cases was 14 per cent.

Dr. Franseen's statistics re-emphasized the lack of correlation between palpability of neck nodes and malignancy, for in only 1 out of 8 cases with palpable nodes were they positive, whereas the nodes were malignant in 3 of 5 cases with prophylactic neck dissections.

Dr. Thomas Anglem, representing the Pondville Hospital, reported on 109 primary cases. The grade of malignancy in this series also seemed essentially unimportant in regard to prognosis. Thirty-eight per cent of the Group 1A cases were cured and none of those in Group 1B, with a total salvage of 11 per cent. Cures by surgery were in the same range as in the other series, namely 31 per cent. The operative mortality was 21 per cent. Radiation cures of 25 per cent were by far the best of any group.

Dr. Channing C. Simmons, chief surgeon of the Huntington Hospital, discussed the papers, pointing out that the end results obtained from the four hospitals were essentially the same. Surgical cases on the whole fared better than those irradiated, even when due consideration was given to operability of the lesions. Lesions situated on the anterior part of the tongue had a better prognosis by either method of treatment, due to their accessibility and lower grade of malignancy. Dr. Simmons emphasized that duration was of little consequence, as in breast cancer, for tumors of low malignancy grow slowly and offer just as favorable if not a more favorable outlook than do the rapidly increasing, highly malignant lesions. The speaker said that irradiation undoubtedly offered a better opportunity for palliation in the inoperable lesions but offered statistics to substantiate his faith in the surgical treatment of operable lesions. Thus 83 per cent of the operable cases were cured of the local lesion, and 60 per cent were totally cured. Dr. Simmons admitted, however, that a sufficient dosage of irradiation had not been given in most instances, and recommended 3000 to 5000 r externally, in addition to local radium or intraoral x-ray.

In the management of the lymph nodes, their size, consistence and movability should be considered, as well as the general condition of the patient and his ability to tolerate the contemplated procedures. Radical operation, Dr. Simmons said, was easier than incomplete neck dis-

section, and all the above surgical mortality figures were given as proof of this statement.

Dr. Simmons concluded that the results depended largely on the facilities at hand, either a good surgeon and anesthetist in the proper environment or a well-trained irradiation expert with the proper equipment. For, although surgery appeared to offer a better chance for cure in these studies, irradiation therapy was rapidly improving and appeared promising.

Dr. W. Martindale Shedden opened the general discussion with a plea for more and better radiation of cervical metastases, on the ground that only 9 per cent of cases were found suitable for radical operation by Duffy of the Memorial Hospital in New York. He stated that better irradiation might conceivably give results comparable to those of surgery.

Dr. Ernest M. Daland assured the audience that the outlook was not so disappointing as it appeared, for treatment was improving and the reported cases were not from the most recent years, since not enough time had elapsed to evaluate the final results.

Dr. George W. Holmes suggested that the high mortality and long delay to treatment reflected the poor selection of cases in clinics, which obviously got the worst cases. He stated that surgery had probably attained its peak and that any improvement would have to come from a better selection of cases for surgery and an advance of irradiation technic, which he said was already occurring. He stated that this community was surgically minded due to its better training in that field than in radiology.

Dr. Anglem summarized the findings of the four investigators from the various institutions. Cancer of the tongue was considered essentially as two entities: those lesions behind the circumvallate papillae which act like pharyngeal lesions and are treated almost exclusively by irradiation, and those lesions on the anterior portion of the tongue which can be treated equally well by adequate surgery or competent irradiation, although past statistics favored the former. Inoperable anterior lesions would receive irradiation as high at least as 10,000 to 12,000 r, one half being given intraorally.

He divided the management of lymph nodes into that relating to the palpable, non-palpable and inoperable groups. It was considered justifiable with non-palpable nodes or those less than 1 cm. in diameter to observe the neck closely rather than to perform a prophylactic dissection. Nodes 1 cm. or larger but movable should be subjected to radical operation only if the patient's general condition is excellent, for the salvage of positive nodes is only 15 or 20 per cent whereas the operative mortality reaches 10 per cent. Dr. Anglem advocated that the alternate treatment with x-rays and interstitial radium be used in some of these so-called operable cases. Inoperable nodes should be treated first with x-rays to decrease their size, and then radium should be implanted in the remnants.

Dr. Anglem reiterated several times the importance of giving large amounts of radiation early and in concentrated doses, so that the cancer can be cured with a minimum degree of deleterious effect on the tumor bed and surrounding blood supply, upon which cure largely depends. He cautioned, however, against the use of large portals, which were responsible for the poor results obtained in former years with large amounts of irradiation.

CONFERENCE ON ENVIRONMENTAL SANITATION

The last in a series of four conferences on environmental sanitation was held at the Department of Public Health, Yale University School of Medicine on Thursday, December 14. The sessions, which were under the auspices of the Department of Public Health in co-operation with the Connecticut State Department of Health, the Connecticut Dairy and Milk Inspectors Association and the Connecticut Public Health Association, were attended by about forty health officers and sanitary inspectors from all parts of Connecticut. Mr. Martin A. Pond, instructor in public health, directed these conferences.

Among the topics discussed were milk sanitation, including inspection of farms and plants, food sanitation, including restaurant and food-manufacturing-establishment inspections, public-health law and problems of water supply, housing, sewage disposal and other sanitation activities. Besides representatives of local health departments and the Connecticut State Department of Health, experts from the United States Public Health Service, the United States Food and Drug Administration and the New York City Department of Health participated in the meetings.

NOTICES

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday evening, January 2, at 8:15.

Dr. Abraham Myerson will speak on "Recent Advances in the Treatment of Epilepsy and Schizophrenia."

MAX RITVO, M.D., *President,*
DAVID B. STEARNS, M.D., *Secretary.*

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a. m.

MEDICAL CONFERENCE PROGRAM, JANUARY-FEBRUARY

Tuesday, January 2 — Thirty Years' Experience in the Treatment of Fractures. Dr. John D. Adams.
Wednesday, January 3 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 4 — Estrogen and Androgen Assay, Indications and Interpretations. Dr. N. T. Werthessen and Dr. C. H. Lawrence.
Friday, January 5 — The Treatment of Epilepsy by Phenobarbital and Dilantin Sodium, and by Various Synergistic Drug Combinations. Dr. Benjamin Cohen.
Saturday, January 6 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 9 — Certain Hematological Problems. Dr. W. Dameshek.
Wednesday, January 10 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 11 — The Place of Electrocardiography in Clinical Diagnosis. Dr. J. M. Faulkner.
Friday, January 12 — The Present-Day Specific Treatment of Pneumonia. Dr. Maxwell Finland.
Saturday, January 13 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 16 — Nephritic Clinic: Presentation of cases. Dr. R. W. Buck.

Wednesday, January 17 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 18 — Surgical Case: Clinicopathological presentation. Dr. H. F. Day.
Friday, January 19 — A Discussion of Rheumatic Fever. Dr. T. Duckett Jones.
Saturday, January 20 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 23 — X-Ray Clinic: Presentation of cases. Dr. A. Ettinger.
Wednesday, January 24 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 25 — Otolaryngology Clinic: Presentation of cases. Dr. P. E. Meltzer.
Friday, January 26 — Peritoneoscopy in Diagnosis of Abdominal Tumors. Dr. W. E. Garrey.
Saturday, January 27 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 30 — Aneurysm and Rupture of the Ventricle of the Heart. Dr. M. N. Fulton.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, January 3, from 2 to 4 p.m. Drs. William C. Quinby and E. A. Stead will speak on "Hematuria." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will take place from 4 to 5 p.m.

On Thursday, January 4, from 8:30 to 9:30 a.m. there will be at the Children's Hospital, a combined clinic, conducted by Dr. William E. Ladd, of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary*.

FAULKNER HOSPITAL CLINICOPATHOLOGICAL CONFERENCE

The monthly clinicopathological conference of the Faulkner Hospital will be held on Thursday, January 4, at 5:00 p.m. Drs. David Halbersleben and G. M. Morrison will discuss cases.

Interested members of the medical profession are invited to attend.

FREE PUBLIC LECTURES

Harvard University has recently announced the subjects and speakers in its course of free public lectures on medical topics that are given each year at the Harvard Medical School. As usual these will be given in the amphitheater of Building D at 4:00 p.m. on Sundays. The schedule is as follows:

January 7. Digestion and Indigestion. Dr. Chester M. Jones.
January 14. Serious Accidents: What to do and what not to do. Dr. Charles C. Lund.
January 21. What About Sulfanilamide? Dr. Chester S. Keefer.
January 28. Care of the Complexion. Dr. Perry C. Baird, Jr.
February 4. Facts and Fancies About Heart Disease. Dr. Paul D. White.
February 11. Cancer. Dr. Grantley W. Taylor.
February 18. The Medical Care of Domestic Pets. Dr. Gerry B. Schnelle.
February 25. Sterility (lecture for women only). Dr. Donald Macomber.
March 3. Backache. Dr. Frank R. Ober.
March 10. Health in Middle Age. Dr. William B. Breed.

CUTTER LECTURES

Dr. Ludvig Hektoen, executive director of the National Advisory Cancer Council of the United States Public Health Service, will give the first of a series of two annual Cutter Lectures in Preventive Medicine at the Harvard Medical School on Monday, January 15. He will talk on the general subject of cancer control with special reference to its public health and epidemiological aspects. The second lecture will be given by Dr. James B. Murphy, member of the Rockefeller Institute for Medical Research, on Monday, January 22. Dr. Murphy will give a critical review of experimental studies in cancer.

Both lectures will be held at 5:00 p.m. in Amphitheater E at the Harvard Medical School. The medical profession, medical and public-health students and others interested are invited to attend.

SALEM HOSPITAL PUBLIC HEALTH LECTURES

The Salem Hospital will conduct a series of Sunday afternoon lectures this winter on medical subjects of general public interest. The purpose of these lectures is to afford the layman an opportunity to gain an accurate knowledge of methods for the protection of his health and the prevention of illness.

The lectures will be free to the public and will be held in the auditorium of the Salem Hospital during January and February, at 4:00 p.m.

The program is as follows:

January 7. New Weapons Against Disease. Dr. Stuart N. Gardner.
January 14. Abuse of Household Gadgets. Dr. Walter G. Phippen.
January 21. Infantile Paralysis. Dr. Edwin D. Reynolds.
January 28. Work and Leisure. Dr. William V. McDermott.
February 4. Anemia and Blood Transfusions. Dr. J. Robert Shaughnessy.
February 11. Health of the School Child. Dr. Charles H. Hogan.
February 18. Obstetrical Facts and Fancies. Dr. Benjamin D. Cornwall.
February 27. Your Eyes. Dr. Henry G. Carroll.

NORFOLK DISTRICT MEDICAL SOCIETY

A special meeting of the councilors of the Norfolk District Medical Society will be held in Sprague Hall in the Boston Medical Library, Wednesday, January 3, at 12 noon.

The call of this meeting is on petition of the West Roxbury Medical Association and its purpose will be to discuss certain forms of group health practice with particular reference to the manner in which such practice may affect the membership of the Norfolk District Medical Society.

Members of the Norfolk District Medical Society who may be interested in the subject are invited to attend and to present their views for the information of the councilors.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

The ninety-ninth semi-annual meeting of the Essex North District Medical Society will be a combined meeting with Essex South District Medical Society and will

be held at the Danvers State Hospital on Wednesday, January 3.

PROGRAM

4:00–5:00 p.m. Ward visits.
5:00–7:00 p.m. Clinic.
7:00 p.m. Dinner. Dr. John S. Hodgson will speak on "Head Injuries."

UNITED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital, Chelsea, will be held at "The Hut," on Friday afternoon, January 12, at 4:00. Dr. Leroy A. Schall will talk, his subject being "Acute Infections of the Upper Respiratory Tract."

JOHN W. TRASK, *Medical Director in Charge.*

AMERICAN SCIENTIFIC CONGRESS

The Eighth American Scientific Congress will be held in Washington, District of Columbia, from May 10 to 18, under the auspices of the Government of the United States of America.

Pursuant to a special act of the Congress of the United States invitations on behalf of the President have been extended to the governments of the American republics that are members of the Pan American Union to participate in the forthcoming meeting. Scientific institutions and organizations are also cordially invited to send representatives.

On April 14, the Pan American Union will celebrate the fiftieth anniversary of its founding. Although the congress will convene a few weeks subsequent to the anniversary date, it will be one of the important phases of that notable celebration. It is hoped that the presence in Washington of many distinguished scientists of all the American republics as participants in this congress will serve as one of the many tributes to the Pan American Union on the occasion of celebrating the completion of a half century of invaluable service in the fostering of good will and better understanding among the republics of the Western Hemisphere.

It has been decided that the congress will be divided into the following sections, each to be in charge of a chairman assisted by a vice-chairman, secretary and section committee: anthropological sciences; biological sciences; geological sciences; agriculture and conservation; public health and medicine; physical and chemical sciences; statistics; history and geography; international law, public law and jurisprudence; economics and sociology; and education.

The chairmen of the respective sections will be selected at an early date, after which the detailed agenda of each section will be announced.

In accordance with established precedent at inter-American conferences, the official languages of the congress will be English, Spanish, Portuguese and French. Papers may be submitted in any one of the official languages and appropriate arrangements will be made for the presentation of the papers, or résumés thereof, in the other official languages of the congress.

The Government of the United States of America attaches particular significance to the forthcoming congress as an important factor in the promotion of co-operative effort among the governments and peoples of the Americas. It is sincerely hoped that prominent scientists throughout the continent may be in a position to contribute to the achievements of the congress by bringing to the discussions the wealth of their knowledge and experience, while enjoying the opportunity of renewing old and making new friendships among the other delegates present on this occasion.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JANUARY 1

TUESDAY, JANUARY 2

*9–10 a.m. Thirty Years' Experience in the Treatment of Fractures. Dr. John D. Adams. Joseph H. Pratt Diagnostic Hospital.
*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.
8:15 p.m. Greater Boston Medical Society. Auditorium, Beth Israel Hospital.

WEDNESDAY, JANUARY 3

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
*12 m. Clinicopathological conference. Children's Hospital amphitheater.
12 m. Norfolk District Medical Society. Boston Medical Library, 8 Fenway, Boston.
*2 p.m.–4 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.

THURSDAY, JANUARY 4

*8:30 a.m.–9:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.
*9–10 a.m. Estrogen and Androgen Assay. Indications and Interpretations. Dr. N. T. Werthessen and Dr. C. H. Lawrence. Joseph H. Pratt Diagnostic Hospital.
*5 p.m. Faulkner Hospital clinicopathological conference.

FRIDAY, JANUARY 5

*9–10 a.m. The Treatment of Epilepsy by Phenobarbital and Dilantin Sodium, and by Various Synergistic Drug Combinations. Dr. Benjamin Cohen. Joseph H. Pratt Diagnostic Hospital.
*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.
12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital. Ether Dome.
*12 m. Urological conference at the Massachusetts General Hospital, lower amphitheater, Out-Patient Department.

SATURDAY, JANUARY 6

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
*10 a.m.–12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.

SUNDAY, JANUARY 7

4 p.m. Digestion and Indigestion. Dr. Chester M. Jones. Free public lecture. Harvard Medical School, amphitheater of Building D.

*Open to the medical profession.

DECEMBER 29 and 30 — Phi Delta Epsilon. Page 918, issue of December 7.

JANUARY 2 — Greater Boston Medical Society. Page 1041.

JANUARY 2–30 — Joseph H. Pratt Diagnostic Hospital, Medical Conference Program. Page 1041.

JANUARY 3 — Metropolitan State Hospital. Clinicopathological conference. Page 1001, issue of December 21.

JANUARY 4 — Faulkner Hospital. Clinicopathological conference. Page 1042.

JANUARY 3 — Peter Bent Brigham Hospital. Joint medical and surgical clinic. Page 1042.

JANUARY 4 — Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital. Page 1042.

JANUARY 5 — United States Marine Hospital. Page 1001, issue of December 21.

JANUARY 6, JUNE 8–11 — American Board of Obstetrics and Gynecology. Page 160, issue of July 27, and page 798, issue of November 16.

JANUARY 7–FEBRUARY 27 — Salem Hospital Public Health Lectures. Page 1042.

JANUARY 7–MARCH 10 — Free Public Lectures, Harvard Medical School. Page 1042.

JANUARY 11 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

JANUARY 12 — United States Marine Hospital. Notice above.

JANUARY 15 and 22 — Cutter Lectures. Page 1042.

JANUARY 22–25 — American Academy of Orthopaedic Surgeons. Hotel Statler, Boston.

FEBRUARY 11–14 — International College of Surgeons. Page 759, issue of November 9.

FEBRUARY 22–24 — American Orthopsychiatric Association. Page 957, issue of December 14.

MARCH 2, JUNE 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

MARCH 7–9 — The New England Hospital Association. Hotel Statler, Boston.

MAY 10–18 — American Scientific Congress. Notice above.

MAY 14 — Pharmacopoeial Convention. Page 894, issue of May 25.

JUNE 7–9 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3 — Semi-annual meeting. Combined meeting with Essex South. Danvers State Hospital, Hathorne. 7 p.m. Page 1042.

ESSEX SOUTH

JANUARY 3 — Head Injuries. Dr. John S. Hodgson. Danvers State Hospital, Hathorne.

FEBRUARY 14 — Cough, Sputum, Hemoptysis — How shall they be investigated? Dr. Reeve H. Betts. Essex Sanatorium, Middleton.

MARCH 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections. Dr. Champ Lyons. Lynn Hospital, Lynn.

APRIL 3 — Addison Gilbert Hospital, Gloucester.

MAY 8 — Annual meeting. Salem Country Club, Peabody.

HAMPSHIRE

JANUARY 10.

MARCH 13.

MAY 8.

All meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

JANUARY 10.

MARCH 20.

MAY 15.

Meetings are held at 12:15 p.m. at the Unicorn Country Club, Stoneham.

MIDDLESEX NORTH

JANUARY 31.

APRIL 24.

JULY 31.

OCTOBER 30.

NORFOLK

JANUARY 3 — Page 1042.

NORFOLK SOUTH

JANUARY 4.

FEBRUARY 1.

MARCH 7.

APRIL 4.

MAY 2.

All meetings, with the exception of one which is usually held at the Quincy City Hospital, are held at the Norfolk County Hospital in South Braintree, at 12 o'clock noon.

PLYMOUTH

JANUARY 18 — Brockton Hospital, Brockton.

MARCH 21 — Goddard Hospital, Brockton.

APRIL 18 — State Farm.

MAY 16 — Lakeville Sanatorium, Lakeville.

SUFFOLK

JANUARY 31 — Scientific meeting. Subject to be announced later.

MARCH 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

WORCESTER

JANUARY 10 — Worcester City Hospital.

FEBRUARY 14 — Worcester State Hospital.

MARCH 13 — Worcester Memorial Hospital.

APRIL 10 — Worcester Hahnemann Hospital.

MAY 8 — Worcester Country Club.

Each meeting begins with a dinner at 6:30 p.m. and is followed by a business and scientific meeting.

BOOK REVIEWS

Pneumonia: With special reference to pneumococcus lobar pneumonia. Roderick Heffron. 1086 pp. New York: The Commonwealth Fund, 1939. $4.50.

Everyone knows that pneumonia is as important an infection as there is: costly, of high mortality, and yet becoming increasingly amenable to treatment as more is learned of the disease and its peculiarities. The ordinary medical textbook does the best it can to describe the treatment of pneumococcal infection. It is a difficult matter, however, to do justice to so important a subject in thirty or forty pages: and this is about the amount of space usually allotted.

Dr. Heffron's book is an admirable piece of work, done with painstaking thoroughness. The fact that there are 1471 references cited in the bibliography is an indication of how carefully the work of other investigators has been considered. And, of course, Dr. Heffron's own contributions to the pneumonia problem in Massachusetts are well known not only in New England but all over the United States.

The book is well written and well printed. The illustrations and tables are easily understandable. The arrangement of the contents is excellent: one easily can find in the text anything about pneumonia from a description of abortive pneumonia at the beginning of the alphabet to x-ray treatment of pneumonia at the end. The clinical aspects of pneumonia, its bacteriology, how immunity is established, what can be done to prevent pneumonia, all receive due consideration. The treatment of pneumonia with serum, vaccine and chemicals is discussed most thoroughly, including nicely written descriptions of how to do things: for example, the best technic for typing, for the administration of serum or for the use of sulfanilamide and allied agents.

In the preface Dr. Heffron states that this book was written to present a comprehensive discussion of pneumonia with special reference to pneumococcal lobar pneumonia and measures for its treatment. He has accomplished his purpose most skilfully. Hospital and medical school libraries will wish to have a copy of this book for reference. Doctors and medical students will wish to own it, because it tells so clearly what to do for the individual patient ill with pneumonia or any of its complications.

Sketches in Psychosomatic Medicine. Nervous and Mental Disease Monograph. No. 65. Smith E. Jelliffe. 155 pp. New York: Nervous and Mental Disease Publishing Company, 1939. $3.00.

All the papers in this book have previously appeared in medical journals. They now are produced in a convenient form as a brief monograph. The entire series is devoted to the exposition of the Freudian explanation of certain bodily signs and the effect of the emotions on physical symptoms. The author is a sound devotee of psychoanalysis and places his material before the medical profession in an expert manner. The book should be widely read for it is a clear presentation of the psychoanalytical viewpoint. References are given to the important literature. There are a few diagrams as illustrations, and the book has an index. Perhaps the most important paper in the whole book is that on the bodily organs in psychopathology, in which the author summarizes his views on the subject.

ERRATUM

Due to a misplaced slug, the last line in Dr. Thomas B. Quigley's article, "Biliary Surgery in the Aged," on page 974 of the December 21 issue of the *Journal* is incorrect. It should read: "biliary disease is discussed." On request, the *Journal* will forward a slip with the correct line for inserting or pasting in the bound volume. — ED.